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09/23/99

UTILITY PATENT APPLICATION TRANSMITTAL <i>(Only for new nonprovisional applications under 37 C.F.R. 1.53(b))</i>	Attorney Docket No.	WHI9721p3MC2
	First Named Inventor or Application Identifier	Andreas Stahl
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16675 U.S. PTO
09/405504

Title of Invention	FATTY ACID TRANSPORT PROTEINS
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APPLICATION ELEMENTS See MPEP chapter 600 concerning utility patent application contents.	ADDRESS TO: Assistant Commissioner for Patents Box Patent Application Washington, D.C. 20231
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1. <input type="checkbox"/> Fee Transmittal Form <i>(Submit an original, and a duplicate for fee processing)</i> 2. <input checked="" type="checkbox"/> Specification [Total Pages <u>115</u>] <i>(preferred arrangement set forth below)</i> - Descriptive title of the invention - Cross References to Related Applications - Statement Regarding Fed sponsored R & D - Reference to microfiche Appendix - Background of the Invention - Summary of the Invention - Brief Description of the Drawings - Detailed Description - Claim(s) - Abstract of the Disclosure 3. <input checked="" type="checkbox"/> Drawing(s) (35 U.S.C. 113) [Total Sheets <u>122</u>] Formal <input type="checkbox"/> Informal <input checked="" type="checkbox"/> 4. <input type="checkbox"/> Oath or Declaration/POA [Total Pages <u> </u>] a. <input type="checkbox"/> Newly executed (original or copy) b. <input type="checkbox"/> Copy from a prior application (37 C.F.R. 1.63(d)) <i>(for continuation/divisional with Box 17 completed)</i> [NOTE Box 5 below] i. <input type="checkbox"/> DELETION OF INVENTOR(S) Signed statement attached deleting inventor(s) named in the prior application, see 37 C.F.R. 1.63(d)(2) and 1.33(b). 5. <input type="checkbox"/> Incorporation By Reference <i>(useable if Box 4b is checked)</i> The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.	6. <input type="checkbox"/> Microfiche Computer Program <i>(Appendix)</i> 7. <input type="checkbox"/> Nucleotide and/or Amino Acid Sequence Submission <i>(if applicable, all necessary)</i> a. <input type="checkbox"/> Computer Readable Copy b. <input type="checkbox"/> Paper Copy (identical to computer copy) c. <input type="checkbox"/> Statement verifying identity of above copies
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ACCOMPANYING APPLICATION PARTS	
8. <input type="checkbox"/> Assignment Papers (cover sheet & documents)	
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17. If a **CONTINUING APPLICATION**, check appropriate box and supply the requisite information:

☐ Continuation ☐ Divisional ☒ Continuation-in-part (CIP) of prior application No.: 09 / 232,201

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Attorney's Docket No.: WHI97-21p3MC2

FATTY ACID TRANSPORT PROTEINS

RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Patent Application Number 09/232,201 filed January 14, 1999, which claims the benefit of U.S. Provisional
5 Application No. 60/110,941 filed December 4, 1998; U.S. Provisional Application No. 60/093,491 filed July 20, 1998; and U.S. Provisional Application No. 60/071,374 filed January 15, 1998. The teachings of each of these referenced applications are incorporated herein by reference in their entirety.

GOVERNMENT SUPPORT

10 The invention was supported, in whole or in part, by a grant from the National Heart, Lung, and Blood Institute (HL41484), by National Institutes of Health Grant DK 47618 and National Institutes of Health Grant 5 T32 CA 09541. The United States Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

15 Long chain fatty acids (LCFAs) are an important source of energy for most organisms. They also function as blood hormones, regulating key metabolic functions such as hepatic glucose production. Although LCFAs can diffuse through the hydrophobic core of the plasma membrane into cells, this nonspecific transport cannot account for the high affinity and specific transport of LCFAs exhibited by cells such as

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cardiac muscle, hepatocytes, enterocytes, and adipocytes. The molecular mechanisms of LCFA transport remains largely unknown. Identifying these mechanisms can lead to pharmaceuticals that modulate fatty acid uptake by the intestine and by other organs, thereby alleviating certain medical conditions (e.g. obesity).

5 SUMMARY OF THE INVENTION

Described herein is a diverse family of fatty acid transport proteins (FATPs) which are evolutionarily conserved; these FATPs are plasma membrane proteins which mediate transport of LCFAs across the membranes and into cells. Members of the FATP family described herein are present in a wide variety of organisms, from mycobacteria to humans, and exhibit very different expression patterns in tissues among the organisms. FATP family members are expressed in prokaryotic and eukaryotic organisms and comprise characteristic amino acid domains or sequences which are highly conserved across family members. In addition, the function of the FATP gene family is conserved throughout evolution, as shown by the fact that the *Caenorhabditis* (C). *elegans* and mycobacterial FATPs described herein facilitate LCFA uptake when they are overexpressed in COS cells or *Escherichia* (E.) *coli*, respectively. FATPs are expressed in a wide variety of tissues, including all tissues which are important to fatty acid metabolism (uptake and processing).

In specific embodiments, FATPs of the present invention are from such diverse organisms as humans (*Homo* (H.) *sapiens*), mice, (*Mus* (M.) *musculus*), *F. rubripes*, *C. elegans*, *Drosophila* (D.) *melanogaster*, *Saccharomyces* (S.) *cerevisiae*, *Aspergillus nidulans*, *Cochliobolu heterostrophus*, *Magnaporthe grisea* and *Mycobacterium* (M.), such as *M. tuberculosis*. As described herein, four novel mouse FATPs, referred to as mmFATP2, mmFATP3, mmFATP4 and mmFATP5, and six human FATPs, referred to as hsFATP1, hsFATP2, hsFATP3, hsFATP4, hsFATP5 and hsFATP6, have been identified. All four novel murine FATPs (mmFATP2-5) and a previously identified murine FATP (renamed herein FATP1) have orthologs in humans (hsFATP1-5); the

sixth human FATP (hsFATP6) does not as yet have a mouse ortholog. The expression patterns of these FATPs vary, as described in detail below.

The present invention relates to FATP family members from prokaryotes and eukaryotes, nucleic acids (DNA, RNA) encoding FATPs, and nucleic acids which are
5 useful as probes or primers (e.g., for use in hybridization methods, amplification methods) for example, in methods of detecting FATP-encoding genes, producing FATPs, and purifying or isolating FATP-encoding DNA or RNA. Also the subject of this invention are antibodies (polyclonal or monoclonal) which bind an FATP or
10 FATPs; methods of identifying additional FATP family members (for example, orthologs of those FATPs described herein by amino acid sequence) and variant alleles of known FATP genes; methods of identifying compounds which bind to an FATP, or modulate or alter (enhance or inhibit) FATP function; compounds which modulate or alter FATP function; methods of modulating or altering (enhancing or inhibiting) FATP function and, thus, LCFA uptake into tissues of a mammal (e.g. human) by
15 administering a compound or molecule (a drug or agent) which increases or reduces FATP activity; and methods of targeting compounds to tissues by administering a complex of the compound to be targeted to tissues and a component which is bound by an FATP present on cells of the tissues to which the compound is to be targeted. For example, a complex of a drug to be delivered to the liver and a component which is
20 bound by an FATP present on liver cells (e.g., FATP5) can be administered.

In one embodiment, the present invention relates to modulating or altering (enhancing or inhibiting/reducing) LCFA uptake in the small intestine and, thus, increasing or reducing the number of calories in the form of fats available to an individual. In another embodiment, the present invention relates to inhibiting or
25 reducing LCFA uptake in the small intestine in order to reduce circulating fatty acid levels; that is, LCFA uptake in the small intestine is reduced and, therefore, circulating (blood) levels are not as high as they otherwise would be. FATP4 has been shown to be expressed in epithelial cells of the small intestine and particularly in the brush border layer of the small intestine. FATP2 has also been shown to be expressed at low levels

in epithelial cells of the small intestine, particularly in the duodenum. In contrast, FATP1, FATP3, FATP5 and FATP6 were not detected in any of the intestinal tissues. Thus, also described herein are FATPs which are present in the epithelial cell layer of the small intestine where they mediate LCFA uptake. These FATPs, particularly

5 FATP4 and also FATP2, are targets for methods and drugs which block their function or activity and are useful in treating obesity, diabetes and heart disease. The ability of these FATPs to mediate fat uptake can be modulated or altered (enhanced or inhibited), thus modulating fat uptake in the small intestine. This can be done, for example, by administering to an individual, such as a human or other animal, a drug which blocks

10 interaction of LCFAs with FATP4 and/or FATP2 in the small intestine, thus inhibiting LCFA passage into the cells of the small intestine. As a result, fat absorption is reduced and, although the individual has consumed a certain quantity of fat, the LCFAs are not absorbed to the same extent they would have been in the absence of the compound administered.

15 Thus, one embodiment of this invention is a method of reducing LCFA uptake (absorption) in the small intestine and, as a result, reducing caloric uptake in the form of fat. A further embodiment is a compound (drug) useful in inhibiting or reducing fat absorption in the small intestine. In another embodiment, the invention is a method of reducing circulating fatty acid levels by administering to an individual a compound

20 which blocks interactions of LCFAs with FATP4 and/or FATP2 in the small intestine, thus inhibiting LCFA passage into cells of the small intestine. As a result, fatty acids pass into the circulatory system at a diminished level and/or rate, and circulating fatty acid levels are lower than they would be in the absence of the compound administered. This method is particularly useful for therapy in individuals who are at risk for or have

25 hyperlipidemia. That is, it can be used to prevent the occurrence of elevated levels of lipids in the blood or to treat an individual in whom blood lipid levels are elevated. Also the subject of this invention is a method of identifying compounds which alter FATP function (and thus, in the case of FATP2 and/or FATP4, alter LCFA uptake in the small intestine).

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In another embodiment, the present invention relates to a method of modulating or altering (enhancing or inhibiting) the function of FATP6, which is expressed at high levels in the heart. A method of inhibiting FATP6 function is useful, for example, in individuals with heart disease, such as ischemia, since reducing LCFA uptake into heart muscle in an individual who has ischemic heart disease, which may be manifested by, for example, angina or heart attack, can reduce symptoms or reduce the extent of damage caused by the ischemia. In this embodiment, a drug which inhibits FATP6 function is administered to an individual who has had or is having a heart attack, to reduce LCFA uptake by the individual's heart and, as a result, reduce the damage caused by ischemia. In a further embodiment, this invention is a method of targeting a compound, such as a therapeutic drug or an imaging reagent, to heart tissue by administering to an individual (e.g., a human) a complex of the compound and a component (e.g., a LCFA or LCFA-like compound) which is bound by an FATP (e.g., FATP6) present in cells of heart tissue.

In a further embodiment, LCFA uptake by the liver is modulated or altered (enhanced or reduced), in an individual. For example, a drug which inhibits the function of an FATP present in liver (e.g., FATP5) is administered to an individual who is diabetic, in order to reduce LCFA uptake by liver cells and, thus reduce insulin resistance.

The present invention, thus, provides methods which are useful to alter, particularly reduce, LCFA uptake in individuals and, as a result, to alter (particularly reduce), availability of the LCFAs for further metabolism. In a specific embodiment, the present invention provides methods useful to reduce LCFA uptake and, thus, fatty acid metabolism in individuals, with the result that caloric availability from fats is reduced, and circulating fatty acid levels are lower than they otherwise would be. These methods are useful, for example, as a means of weight control in individuals, (e.g., humans) and as a means of preventing elevated serum lipid levels or reducing serum lipid levels in humans. FATPs expressed in the small intestine, such as FATP4, are useful targets to be blocked in treating obesity (e.g., chronic obesity) or to be enhanced

in treating conditions in which enhanced LCFA uptake is desired (e.g., malabsorption syndrome or other wasting conditions).

The identification of this evolutionarily conserved fatty acid transporter family will allow a better understanding of the mechanisms whereby LCFAs traverse the lipid bilayer as well as yield insight into the control of energy homeostasis and its dysregulation in diseases such as diabetes and obesity.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the amino acid sequence alignment of FATPs: mmFATP1 (SEQ ID NO:92), mmFATP2 (SEQ ID NO:93), mmFATP3 (SEQ ID NO:94), mmFATP4 (SEQ ID NO:95), mmFATP5 (SEQ ID NO:96), ceFATPa (SEQ ID NO:97), scFATP (SEQ ID NO:98) and mtFATP (SEQ ID NO:99). The underlining (amino acid residues 204-212 of mtFATP) indicates an AMP binding motif which is found in many classes of proteins; the underlining at amino acid residues 204-507 of the mtFATP sequence indicates the FATP 360 amino acid signature sequence.

Figures 2A-2D show results of LCFA uptake assays. Figures 2A-2D: COS cells were cotransfected using the DEAE-dextran method with the mammalian expression vectors pCDNA-CD2 either alone (control; Figure 2A) or in combination with one of the FATP-containing expression vectors (pCDNA-mmFATP1, Figure 2B; pCDNA-mmFATP2, Figure 2C; or pCMV-SPORT2-mmFATP5, Figure 2D) as described in Materials and Methods for Example 2. COS cells were gated on forward scatter (FSC) and side scatter (SS), and the results shown represent >10,000 cells. Cells exhibiting >300 CD2 fluorescence units (vertical line) representing 15% of all cells were deemed CD2 positive.

Figure 3 is a graph of fluorescence of cells expressing a FATP gene. As in Figures 2A-2D, COS cells were cotransfected with pCDNA-CD2 either alone (control) or in combination with one of the FATP-containing expression vectors (pCDNA-mmFATP1, pCDNA-mmFATP2, pCMV-SPORT2-mmFATP5, or pCDNA-ceFATPb). The mean BODIPY-FA fluorescence of the CD2-positive cells is plotted; results shown

represent the average of three experiments, each consisting of greater than 50,000 COS cells. Note that a logarithmic scale is used on the ordinate.

Figure 4 is a graph of the uptake of palmitate with time. The full-length coding region of mtFATP (squares) or a control protein (TFE3; circles) was subcloned into the inducible, prokaryotic expression vector pET (Novagen). Expression from the resulting plasmid was induced (solid symbols) in transformed *E. coli* cells with 1 mM isopropyl- β -D-thiogalactoside (IPTG) for 1 hour, or cells were left uninduced (open symbols). Data points were done in triplicate and counts were normalized to the number of bacteria as determined by OD₆₀₀.

Figure 5 is a phylogenetic tree produced by aligning complete and partial sequences for *FATP* genes from human, rat, mouse, puffer fish, *D. melanogaster*, *C. elegans*, *S. cerevisiae*, and *M. tuberculosis* using ClustalX and using these data to produce a phylogenetic tree using TreeViewPPC. The bar indicates the number of substitutions per residue, i.e., 0.1 corresponds to a distance of 10 substitutions per 100 residues.

Figure 6 shows a comparison of the FATP signature sequences of mmFATP1 (SEQ ID NO:1), mmFATP5, (SEQ ID NO:2), ceFATPa (SEQ ID NO:3), scFATP (SEQ ID NO:4) and mtFATP (SEQ ID NO:5).

Figure 7 shows the sequence identity among the FATP family members and VLACs, based on the 360 amino acid signature sequence of FATP from Figure 1.

Figures 8A and 8B are the mmFATP3 DNA sequence (SEQ ID NO:6).

Figure 9 is the mmFATP3 protein sequence (SEQ ID NO:7).

Figures 10A and 10B are the mmFATP4 DNA sequence (SEQ ID NO:8).

Figure 11 is the mmFATP4 protein sequence (SEQ ID NO:9).

Figures 12A and 12B are the mmFATP5 DNA sequence (SEQ ID NO:10).

Figure 13 is the mmFATP5 protein sequence (SEQ ID NO:11).

Figures 14A and 14B are the hsFATP2 DNA sequence (SEQ ID NO:12).

Figure 15 is the hsFATP2 protein sequence (SEQ ID NO:13).

Figures 16A and 16B are the hsFATP3 DNA sequence (SEQ ID NO:14).

Figure 17 is the hsFATP3 protein sequence (SEQ ID NO:15).

Figures 18A and 18B are the hsFATP4 DNA sequence (SEQ ID NO:16).

Figure 19 is the hsFATP4 protein sequence (SEQ ID NO:17).

Figures 20A and 20B are the hsFATP5 DNA sequence (SEQ ID NO:18).

5 Figure 21 is the hsFATP5 protein sequence (SEQ ID NO:19).

Figures 22A and 22B are the hsFATP6 DNA sequence (SEQ ID NO:20).

Figure 23 is the hsFATP6 protein sequence (SEQ ID NO:21).

Figures 24A and 24B are the mtFATP DNA sequence (SEQ ID NO:22).

Figure 25 is the mtFATP protein sequence (SEQ ID NO:23).

10 Figure 26 shows the DNA sequence (SEQ ID NO:24) and predicted amino acid sequence (SEQ ID NO:25) of human FATP1.

Figure 27 shows the DNA sequence (SEQ ID NO:26) and predicted amino acid sequence (SEQ ID NO:27) of human FATP4.

15 Figure 28A is a hydrophobicity plot for hsFATP1, showing that it has multiple membrane-spanning domains.

Figure 28B is the amino acid composition of hsFATP1.

Figure 28C is a hydrophilicity plot for hsFATP1, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

20 Figure 29A is a hydrophobicity plot for hsFATP4, showing that it has multiple membrane-spanning domains.

Figure 29B is a listing of the amino acid composition of hsFATP4.

Figure 29C is a hydrophilicity plot for hsFATP4, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

25 Figures 30A and 30B show a comparison of the nucleotide sequence of human FATP1 (SEQ ID NO:28) and the nucleotide sequence of mouse FATP1 (SEQ ID NO:29).

Figures 31A and 31B show a comparison of the nucleotide sequence of human FATP4 (SEQ ID NO:30) and the nucleotide sequence of mouse FATP4 (SEQ ID NO:31).

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Figure 32 shows a comparison of the amino acid sequence of human FATP1 (SEQ ID NO:32) and the amino acid sequence of mouse FATP1 (SEQ ID NO:33).

Shaded amino acid residues match the consensus sequence exactly

Figure 33 shows a comparison at the amino acid level of human FATP4 (SEQ ID NO:34) and mouse FATP4 (SEQ ID NO:35). Shaded amino acid residues match the consensus sequence exactly.

Figure 34 shows the nucleotide sequence (SEQ ID NO:36) and predicted amino acid sequence (SEQ ID NO:37) of hsFATP6.

Figure 35A is a hydrophobicity plot for hsFATP6, showing that it has multiple membrane-spanning domains.

Figure 35B is a listing of the amino acid composition of hsFATP6.

Figure 35C is a hydrophilicity plot for hsFATP6, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 36 shows an alignment of the amino acid sequences of hsFATP1 (SEQ ID NO:38), hsFATP4 (SEQ ID NO:39) and hsFATP6 (SEQ ID NO:40). Shaded amino acid residues match the consensus sequence exactly.

Figure 37 shows results of assessment of fatty acid uptake by human FATP1 and human FATP4. The percent of CD2-positive cells exhibiting a BODIPY-fluorescence of more than 300 arbitrary units is plotted for the three different conditions tested.

Figure 38 is a graph showing uptake of tritiated oleate, with time, by 293 cells transfected with either (diamonds) a plasmid for expression of human FATP4 or (squares) a control plasmid.

Figure 39 is an illustration of the amino acid sequences of human FATP4 (SEQ ID NO:41) and mouse FATP4 (SEQ ID NO:42) compared to human FATP1 (SEQ ID NO:43). Shown by underlining are the FATP consensus sequence (236-556 of hsFATP1) and the AMP-binding motif (246-254 of hsFATP1). The human FATPs were cloned by screening libraries with sequences from ESTs (expressed sequence tags). Mouse FATP4 was cloned by PCR using degenerate primers.

Figure 40 is a graph showing the uptake, with time, of tritiated oleate by mouse enterocytes in the presence of no oligonucleotide (squares), sense oligonucleotide (circles) or antisense oligonucleotide (diamonds).

Figure 41 is a bar graph showing uptake of tritiated oleate, by mouse enterocytes
5 in the presence of various concentrations of antisense (solid bars), mismatch (stippled bars) or sense (lined bars) oligonucleotides.

Figure 42 is a bar graph showing uptake of tritiated oleate and uptake of ³⁵S-labeled methionine by mouse enterocytes to which were added no oligonucleotide, the antisense oligonucleotide, or the mismatch oligonucleotide.

10 Figure 43A is the nucleotide sequence of the gene encoding mouse FATP4 (SEQ ID NO:44).

Figure 43B is the amino acid sequence of mouse FATP4 protein (SEQ ID NO:45).

Figures 44A, 44B, and 44C are the hsFATP1 DNA sequence (SEQ ID NO:46).
15 Coding region: 175-2115 (1941 nt).

Figure 45 is the hsFATP1 protein sequence (SEQ ID NO:47).

Figures 46A and 46B are the hsFATP2 DNA sequence (SEQ ID NO:48).
Coding region: 223-2085 (1863 nt).

Figure 47 is the hsFATP2 protein sequence (SEQ ID NO:49).

20 Figure 48 is the partial DNA sequence of hsFATP3 (SEQ ID NO:50). Coding region: 1-993.

Figure 49 is the partial protein sequence of hsFATP3 (SEQ ID NO:51).

Figures 50A, 50B, and 50C are the hsFATP4 DNA sequence (SEQ ID NO:52).
Coding region: 208-2139 (1932 nt).

25 Figure 51 is the hsFATP4 protein sequence (SEQ ID NO:53).

Figure 52 is the hsFATP5 partial DNA sequence (SEQ ID NO:54). Coding region: 1-1062.

Figure 53 is the hsFATP5 partial protein sequence (SEQ ID NO:55).

Figures 54A, 54B, and 54C are the hsFATP6 DNA sequence (SEQ ID NO:56).
Coding region: 643-2502 (1860 nt).

Figure 55 is the hsFATP6 protein sequence (SEQ ID NO:57).

Figures 56A, 56B, and 56C are the mFATP1 DNA sequence (rn=*Rattus*
5 *norvegicus*; (SEQ ID NO:58). Coding region: 75-2015 (1941 nt).

Figure 57 is the mFATP1 protein sequence (SEQ ID NO:59).

Figure 58A, 58B, and 58C are the mFATP2 DNA sequence (SEQ ID NO:60).
Coding region: 795-2657 (1863 nt).

Figure 59 is the mFATP2 protein sequence (SEQ ID NO:61).

10 Figure 60A and 60B are the mFATP4 partial DNA sequence (SEQ ID NO:62).
Coding region: 1-1218.

Figure 61 is the mFATP4 partial DNA sequence (SEQ ID NO:63).

Figure 62A, 62B, and 62C are the mmFATP1 DNA sequence (SEQ ID NO:64).
Coding region: 1-1944.

15 Figure 63 is the mmFATP1 protein sequence (SEQ ID NO:65).

Figures 64A and 64B are the mmFATP2 DNA sequence (SEQ ID NO:66).
Coding region: 121-1992 (1872 nt).

Figure 65 is the mmFATP2 protein sequence (SEQ ID NO:67).

Figures 66A and 66B are the mmFATP3 partial DNA sequence (SEQ ID
20 NO:68). Coding region: 1-1830.

Figure 67 is the mmFATP3 partial protein sequence (SEQ ID NO:69).

Figures 68A, 68B, and 68C are the mmFATP4 DNA sequence (SEQ ID NO:70).
Coding region: 1-1932.

Figures 69 is the mmFATP4 protein sequence (SEQ ID NO:71).

25 Figures 70A and 70B are the mmFATP5 DNA sequence (SEQ ID NO:72).
Coding region: 60-2129.

Figure 71 is the mmFATP5 protein sequence (SEQ ID NO:73).

Figures 72A and 72B are the dmFATP partial DNA sequence (dm=*Drosophila*
melanogaster; SEQ ID NO:74). Coding region: 1-1773.

Figures 73 is the dmFATP partial protein sequence (SEQ ID NO:75).

Figure 74 is the drFATP partial DNA sequence (dr=*Danio rerio*, zebrafish; SEQ ID NO:76) Coding region: 1-173.

Figure 75 is the drFATP partial protein sequence (SEQ ID NO:77).

5 Figure 76A and 76B are the ceFATPa DNA sequence (SEQ ID NO:78). Coding region: 1-1953.

Figure 77 is the ceFATPa protein sequence (SEQ ID NO:79).

Figures 78A and 78B are the ceFATPb DNA sequence (SEQ ID NO:80). Coding region: 1-1968.

10 Figure 79 is the ceFATPb protein sequence (SEQ ID NO:81).

Figures 80A and 80B are the chFATP DNA sequence (SEQ ID NO:82; ch=*Cochliobolu heterostrophus*). Coding region: 1-1932.

Figure 81 is the chFATP protein sequence (SEQ ID NO:83).

15 Figure 82 is the anFATP partial protein sequence (an=*Aspergillus nidulans*; SEQ ID NO:84). Coding region: 1-597.

Figure 83 is the anFATP partial protein sequence (SEQ ID NO:85).

Figure 84 is the mgFATP partial DNA sequence (mg= *Magnaporthe grisea*, rice blast; SEQ ID NO:86). Coding region: 1-522.

Figure 85 is the mgFATP partial protein sequence (SEQ ID NO:87).

20 Figures 86A and 86B are the scFATP DNA sequence (SEQ ID NO:88). Coding region: 1-1872.

Figure 87 is the scFATP protein sequence (SEQ ID NO:89).

Figures 88A and 88B are the mtFATP DNA sequence (SEQ ID NO:90).

25 Figure 89 is the mtFATP protein sequence (SEQ ID NO:91). Coding region: 1-1794.

Figure 90 is a consensus sequence of the FATP signature sequence (SEQ ID NO:100), based on 23 independent sequences aligned in ClustalX. The height of the bar at each amino acid residue position indicates the degree of conservation at that position. Gaps have been inserted to maintain the strength of the alignment.

Figure 91 is a hydrophilicity plot for hsFATP2, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 92 is a hydrophilicity plot for the hsFATP3 partial protein, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues
5 at a time.

Figure 93 is a hydrophilicity plot for the hsFATP5 partial protein, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figures 94A and 94B are a representation of the DNA sequence (SEQ ID
10 NO:101) of the hsFATP3 gene, and the amino acid sequence (SEQ ID NO:102) of the hsFATP3 protein.

Figure 95. Mammalian expression constructs containing either hsFATP4 (squares and triangles) or empty control vector (circles) were stably transfected into 293 cells. Short-term uptake of Bodipy-FA in the presence of BSA was determined by
15 FACS. The mean fluorescence of the viable cell population is expressed in arbitrary fluorescence units. FATP4 protein expression was determined by densitometry of anti-FATP4 Western blots, and is expressed in arbitrary units.

Figure 96. Short-term uptake of Bodipy-palmitate (1 μ M), either by control cells (black bars) or FATP4-expressing cells (hatched bars), was measured in the
20 presence of 0, 10, 100 μ M unlabeled palmitate. FA uptake was quantified by FACS and expressed in arbitrary fluorescence units.

Figure 97. The rate of [2 H]palmitate uptake by 293 cells, which were stably transfected with a construct for either human FATP4 (diamonds) or an empty vector (circles), was compared to that of isolated enterocytes (squares).

25 Figure 98. Isolated enterocytes were incubated for 48h with increasing concentrations of the FATP4 antisense oligonucleotide or with 100 μ M of a randomized control oligonucleotide with identical nucleotide composition to the FATP4 antisense oligonucleotide. The uptake of oleate by the enterocytes was then measured over a 5 min time interval (solid bars). In parallel, the levels of FATP4 protein and, as a loading

control, β -catenin, were determined by Western blotting and quantitated using densitometry (hatched bars). FA uptake and FATP4 protein levels were normalized to that of untreated cells. The averages and standard deviations of 4 independent experiments are shown.

- 5 Figure 99. Uptake rates of [^3H]oleate, [^3H]palmitate and [^{35}S]methionine by primary enterocytes were measured after 48h incubation with either 100 μM FATP4 antisense (solid bars) or 100 μM randomized control oligonucleotide (hatched bars) and expressed as % of untreated cells.

DETAILED DESCRIPTION OF THE INVENTION

- 10 As described herein, FATPs are a large evolutionarily conserved family of proteins that mediate the transport of LCFAs into cells. The family includes proteins which are conserved from mycobacteria to humans and exhibit very different expression patterns in tissues. Specific embodiments described include FATPs from mice, humans, nematodes, fungi and mycobacteria which have been shown to be functional LCFA
- 15 transporters. The term "fatty acid transport proteins" ("FATPs") as used herein, refers to the proteins described herein as FATP1, FATP2, FATP3, FATP4, FATP5 and FATP6, which have been described in one or more species of mammals, as well as mtFATP, ceFATP, scFATP, anFATP, mgFATP, and chFATP, and other proteins sharing at least about 50% amino acid sequence similarity, preferably at least about 60%
- 20 sequence similarity, more preferably at least about 70% sequence similarity, and still more preferably, at least about 80% sequence similarity, and most preferably, at least about 90% sequence similarity in the approximately 360 amino acid signature sequence. The approximately 360 amino acid FATP signature sequence is shown in Figure 1. The consensus sequence of the signature sequence is shown in Figure 90. The nomenclature
- 25 used herein to refer to FATPs includes a species-specific prefix (e.g., mm, *Mus musculus*; hs or h, *Homo sapiens* or human; mt *M. tuberculosis*; dm. *D. melanogaster*; ce, *C. elegans*; sc, *Saccharomyces cerevisiae*) and a number such that mammalian homologues in different species share the same number. For example, six human and

five mouse *FATP* genes which are expressed in a variety of tissues are described herein and are referred to, respectively, as hsFATP1-hsFATP6 and mmFATP1-mmFATP5; for example, hsFATP4 and mmFATP4 are the human and mouse orthologs.

Expression patterns of human and mouse FATPs have been assessed and are described below. Briefly, results of these assessments show that FATP5 is a liver-specific gene. FATP2 is highly expressed in liver and kidney. Both of these proteins, as well as FATP4 and FATPs from nematodes and mycobacteria, have been shown to be functional LCFA transporters. Results have also shown that FATP4 mRNA is present at high levels in epithelial cells of two regions of the small intestine (the jejunum and ileum) and at lower, but significant, levels in a third region (the duodenum). They further showed that FATP2 mRNA is present in epithelial cells of the duodenum at a level similar to that of FATP4 mRNA levels, but is present at lower levels in the jejunum and ileum. FATP4 mRNA was absent from other cell types of the small intestine and no FATP4 mRNA could be detected in any cells of the colon. No signals above background could be detected for FATP1, FATP3 and FATP5 in any of the intestinal tissues. Thus, FATP4 is the major FATP in the mouse small intestine, which supports a major role for FATP4 (along with FATP2 to a lesser extent) in absorption of free fatty acids. hsFATP4 was clearly expressed in the jejunum and ileum; expression was absent in the stomach. This, too, is consistent with a major role for FATP4 in absorption of fatty acids in the human gut. Analysis of FATP expression in human tissues, also described in detail below, showed that hsFATP6, which has no mouse ortholog as yet, is expressed at high levels in the heart and at low levels in the placenta, but is undetectable in the other tissues assessed (Example 9). This is consistent with a major role for FATP6 in absorption of fatty acids in the heart.

Long chain fatty acids (LCFAs) are an important energy source for pro- and eukaryotes and are involved in diverse cellular processes, such as membrane synthesis, intracellular signaling, protein modification, and transcriptional regulation. In developed Western countries, human dietary lipids are mainly di- and triglycerides and account for approximately 40% of caloric intake (Weisburger, J. H. (1997) *J. Am. Diet.*

Assoc. 97:S16-S23). These lipids are broken down into fatty acids and glycerol by pancreatic lipases in the small intestine (Chapus, C., Ravery, M., Sarda, L & Verger, R. (1988) *Biochimie* 70:1223-34); LCFAs are then transported into brush border cells, where the majority is re-esterified and secreted into the lymphatic system as chylomicrons (Green, P.H. & Riley, J.W. (1981) *Aust. N.Z.J. Med.* 11:84-90). Fatty acids are liberated from lipoproteins by the enzyme lipoprotein lipase, which is bound to the luminal side of endothelial cells (Scow, R.O. & Blachette-Mackie, E.J. (1992) *Mol. Cell. Biochem* 116:181-191). "Free" fatty acids in the circulation are bound to serum albumin (Spector, A.A. (1984) *Clin. Physiol. Biochem* 2:123-134) and are rapidly incorporated by adipocytes, hepatocytes, and cardiac muscle cells. The latter derive 60-90% of their energy through the oxidation of LCFAs (Neely, J.F. Rovetto, M.J. & Oram, J.F. (1972) *Prog. Cardiovasc. Dis:* 15:289-329). Although saturable and specific uptake of LCFAs has been demonstrated for intestinal cells, hepatocytes, cardiac myocytes, and adipocytes, the molecular mechanisms of LCFA transport across the plasma membrane have remained controversial (Hui, T.Y. & Bernlohr, D.A. (1997) *Front. Biosci.* 15:d222-31-d231; Schaffer, J.E. & Lodish, H.F. (1995) *Trends Cardiovasc. Med.* 5:218-224). Described herein is a large family of highly homologous mammalian LCFA transporters which show wide expression, including in all tissues relevant to fatty acid metabolism. Further described are novel members of this family in other species, including mycobacterial and nematode FATPs which, like their mammalian counterparts, are functional fatty acid transporters.

The discovery of a diverse but highly homologous family of FATPs is reminiscent of the glucose transporter family. In a manner similar to the FATPs, the glucose transporters have very divergent patterns of tissue expression (McGowan, K.M., Long, S.D. & Pekala, P.H. (1995) *Pharmacol. Ther.* 66:465-505). The FATPs, like glucose transporters, may also differ in their substrate specificities, uptake kinetics, and hormonal regulation (Thorens, B. (1996) *Am. J. Physiol.* 270:G541-G553). Indeed, the levels of fatty acids in the blood, like those of glucose, can be regulated by insulin and are dysregulated in diseases such as noninsulin-dependent diabetes and obesity (Boden,

G. (1997) *Diabetes* 46:3-10). The underlying mechanisms for the regulation of free fatty acid concentrations in the blood are not understood, but could be explained by hormonal modulation of FATPs.

Insulin-resistance is thought to be the major defect in non insulin-dependent
 5 diabetes mellitus (NIDDM) and is one of the earliest manifestations of NIDDM
 (McGarry (1992) *Science* 258:766-770). Free fatty acids (FFAs) may provide an
 explanation for why obesity is a risk factor for NIDDM. Plasma levels of FFAs are
 elevated in diabetic patients (Reaven *et al.* (1988) *Diabetes* 37:1020). Elevated plasma
 free fatty acids (FFAs) have been demonstrated to induce insulin-resistance in whole
 10 animals and humans (Boden (1998) *Front. Biosci.* 3:D169-D175). This insulin-
 resistance is likely mediated by effects of FFAs on a variety of issues. FFAs added to
 adipocytes *in vitro* induce insulin resistance in this cell type as evidenced by inhibition
 of insulin-induced glucose transport (Van Epps-Fung *et al.* (1997) *Endocrinology*
 138:4338-4345). Rats fed a high fat diet developed skeletal muscle insulin resistance as
 15 evidenced by a decrease in insulin-induced glucose uptake by skeletal muscle (Han *et*
al., (1997) *Diabetes* 46:1761-1767). In addition, elevated plasma FFAs increase
 insulin-suppressed endogenous glucose production in the liver (Boden (1998) *Front.*
Biosci. 3:D169-D175), thus increasing hepatic glucose output. It has been postulated
 that the adverse effects of plasma free fatty acids are due to the FFAs being taken up
 20 into the cell, leading to an increase in intracellular long chain fatty acyl CoA;
 intracellular long chain acyl CoAs are thought to mediate the effects of FFAs inside the
 cell. Thus, fatty acid induced insulin-resistance may be prevented by blocking uptake
 of FFAs into select tissues, in particular liver (by blocking FATP2 and/or FATP5),
 adipocyte (by blocking FATP1), and skeletal muscle (by blocking FATP1). Blocking
 25 intestinal fat absorption (by blocking FATP4) is also expected to reduce plasma FFA
 levels and thus improve insulin resistance.

During the pathogenesis of NIDDM insulin-resistance can initially be
 counteracted by increasing insulin output by the pancreatic beta cell. Ultimately, this
 compensation fails, beta cell function decreases and overt diabetes results (McGarry

(1992) *Science* 258: 766-770). Manipulating beta cell function is a second point where fatty acid transporter blockers may be beneficial for diabetes. While no FATP homolog has been identified so far that is expressed in the beta cell of the pancreas, the data described below suggest the existence of such a transporter and the sequence

5 information included herein provides the means to identify such a transporter by degenerate PCR, using primers to regions conserved in all FATP family members or by low stringency hybridization. It has been demonstrated that exposure of pancreatic beta-cells to FFAs increases the basal rate of insulin secretion; this in turn leads to a decrease in the intracellular stores of insulin, resulting in decreased capacity for insulin
10 secretion after chronic exposure (Bollheimer *et al.*, (1998) *J. Clin. Invest.* 101:1094-1101). The effects of FFAs are again likely to be mediated by intracellular long chain fatty acyl CoA molecules (Liu *et al.*, (1998) *J. Clin. Invest.* 101:1870-1875). FFAs have also been demonstrated to increase beta cell apoptosis (Shimabukuro *et al.*, (1998) *Proc. Nat. Acad. Sci. USA* 95:2498-2502), possibly contributing to the decrease in beta
15 cell numbers in late stage NIDDM.

Another finding with potentially broad implications is the identification of a FATP homologue in *M. tuberculosis*. Tuberculosis causes more deaths worldwide than any other infectious agent and drug-resistant tuberculosis is re-emerging as a problem in industrialized nations (Bloom, B.R. & Small, P.M. (1998) *N. Engl. J. Med.* 338:677-
20 678). *Mycobacterium tuberculosis* has about 250 enzymes involved in fatty acid metabolism, compared with only about 50 in *E. coli*. It has been suggested that, living as a pathogen, the mycobacteria are largely lipolytic, rather than lipogenic, relying on the lipids within mammalian cells and the tubercle (Cole, S.T. *et al.*, *Nature* 393:537-544 (1998)). The *de novo* synthesis of fatty acids in *Mycobacterium leprae* is
25 insufficient to maintain growth (Wheeler, P.R., Bulmer, K & Ratledge, C. (1990) *J. Gene. Microbiol.* 136:211-217). Thus, it is reasonable to expect that inhibitors of mtFATP will serve as therapeutics for tuberculosis. FATPs expressed in mycobacteria can be targeted to reduce or prevent replication of mycobacteria (e.g., to reduce or prevent replication of *M. tuberculosis*) and, thus, reduce or prevent their adverse effects.

For example, a FATP or FATPs expressed by *M. tuberculosis* can be targeted and inhibited, thus reducing or preventing growth of this pathogen (and tuberculosis in humans and other mammals). An inhibitor of an *M. tuberculosis* FATP can be identified, using methods described herein (e.g., expressing the FATP in an appropriate host cell, such as *E. coli* or COS cells; contacting the cells with an agent or drug to be assessed for its ability to inhibit the FATP and, as a result, mycobacterial growth, and assessing its effects on growth). A drug or agent identified in this manner can be further tested for its ability to inhibit a *M. tuberculosis* FATP and *M. tuberculosis* infection in an appropriate animal model or in humans. A method of inhibiting mycobacterial growth, particularly growth of *M. tuberculosis*, and compounds useful as drugs for doing so are also the subject of this invention.

An isolated polynucleotide encoding mtFATP, like other polynucleotides encoding FATPs of the FATP family, can be incorporated into vectors, nucleic acids of viruses, and other nucleic acid constructs that can be used in various types of host cells to produce mtFATP. This mtFATP can be used, as it appears on the surface of cells, or in various artificial membrane systems, to assess fatty acid transport function, to identify ligands and molecules that are modulators of fatty acid transport activity. Molecules found to be inhibitors of mtFATP function can be incorporated into pharmaceutical compositions to administer to a human for the treatment of tuberculosis.

Particular embodiments of the invention are polynucleotides encoding a FATP of *Cochliobolus (Helminthosporium) heterostrophus* or portions or variants thereof, the isolated or recombinantly produced FATP, methods for assessing whether an agent binds to the chFATP, and further methods for assessing the effect of an agent being tested for its ability to modulate fatty acid transport activity. *Cochliobolus heterostrophus* is an ascomycete that is the cause of southern corn leaf blight, an economically important threat to the corn crop in the United States. The related species *C. sativus* causes crown rot and common root rot in wheat and barley. One or more FATPs of *C. heterostrophus* can be targeted for the identification of an inhibitor of chFATP function, which can be then be used as an agent effective against infection of

plants by *C. heterostrophus* and related organisms. Methods described herein that were applied in studying the expression of a FATP gene and the function of the FATP in its natural site of expression or in a host cell, can be used in the study of the chFATP gene and protein.

5 *Magnaporthe grisea* (rice blast) is an economically important fungal pathogen of rice. Further embodiments of the invention are nucleic acid molecules encoding a FATP of *Magnaporthe grisea*, portions thereof, or variants thereof, isolated mgFATP, nucleic acid constructs, and engineered cells expressing mgFATP. Other aspects of the invention are assays to identify an agent which binds to mgFATP and assays to identify
10 an agent which modulates the function of mgFATP in cells in which mgFATP is expressed or in artificial membrane systems. Agents identified as inhibiting mgFATP activity can be developed into anti-fungal agents to be used to treat rice infected with rice blast.

Caenorhabditis elegans is a nematode related to plant pathogens and human
15 parasites. An isolated polynucleotide which encodes ceFATP, like other polynucleotides encoding FATPs of the FATP family described herein, can be incorporated into nucleic acid vectors and other constructs that can be used in various types of cells to produce ceFATP. ceFATP as it occurs in cells or as it can be isolated or incorporated into various artificial or reconstructed membrane systems, can be used
20 to assess fatty acid transport, and to identify ligands and agents that modulate fatty acid transport activity. Agents found by such assays to be inhibitors of ceFATP activity can be incorporated into compositions for the treatment of diseases caused by genetically related organisms with a FATP of similar sensitivity to the agents.

Aspergillus nidulans is one of a family of fungal species that can infect humans.
25 Further embodiments of the invention of the family of polynucleotides encoding FATPs are polynucleotides encoding a FATP of *Aspergillus nidulans*, and vectors and host cells that can be constructed to comprise such polynucleotides. Further embodiments are a polypeptide encoded by such polynucleotides, portions thereof having one or more functions characteristic of a FATP, and various methods. The methods include those

for identifying agents that bind to anFATP and those for assessing the effect of an agent being tested for its ability to modulate fatty acid transport activity. Those agents found to inhibit fatty acid transport function can be used in compositions as anti-fungal pharmaceuticals, or can be modified for greater effectiveness as a pharmaceutical.

5 One aspect of the invention relates to isolated nucleic acids that encode a FATP as described herein, such as those FATPs having an amino acid sequence in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figures 94A and 94B (SEQ ID NO:102), Figure 51 (SEQ ID NO:53), Figure 53 (SEQ ID NO:55), and Figure 55 (SEQ ID NO:57) and nucleic acids closely related thereto as described herein.

10 Using the information provided herein, such as a nucleic acid sequence set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A and 46B (SEQ ID NO:48), Figures 94A and 94B (SEQ ID NO:101), Figures 50A-50C (SEQ ID NO:52), Figure 52 (SEQ ID NO:54), and Figures 54A-54C (SEQ ID NO:56), a nucleic acid of the invention encoding a FATP polypeptide may be obtained using standard cloning and screening
15 methods, such as those for cloning and sequencing cDNA library fragments, followed by obtaining a full length clone. For example, to obtain a nucleic acid of the invention, a library of clones of cDNA of human or other mammalian DNA can be probed with a labeled oligonucleotide, such as a radiolabeled oligonucleotide, preferably about 17 nucleotides or longer, derived from a partial sequence. Clones carrying DNA identical
20 to that of the probe can then be distinguished using stringent (also, "high stringency") hybridization conditions. By sequencing the individual clones thus identified with sequencing primers designed from the original sequence it is then possible to extend the sequence in both directions to determine the full length sequence. Suitable techniques are described, for example, in *Current Protocols in Molecular Biology* (F.M. Ausubel et
25 al, eds), containing supplements through Supplement 42, 1998, John Wiley and Sons, Inc., especially chapters 5, 6 and 7.

Embodiments of the invention include isolated nucleic acid molecules comprising any of the following nucleotide sequences: 1.) a nucleotide sequence which encodes a protein comprising the amino acid sequence of hsFATP1 (SEQ ID

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NO:47), the amino acid sequence of hsFATP2 (SEQ ID NO:49), the amino acid sequence of hsFATP3 (SEQ ID NO:51), the amino acid sequence of hsFATP4 (SEQ ID NO: 53), the amino acid sequence of hsFATP5 (SEQ ID NO:55) or the amino acid sequence of hsFATP6 (SEQ ID NO:57); 2.) nucleotide sequences of hsFATP1, 5 hsFATP2, hsFATP3, hsFATP4, hsFATP5, or hsFATP6 (SEQ ID NO:46, 48, 101, 52, 54, or 56, respectively); 3.) a nucleotide sequence which is complementary to the nucleotide sequence of hsFATP1 (SEQ ID NO:46), hsFATP2 (SEQ ID NO:48), hsFATP3 (SEQ ID NO:101), hsFATP4 (SEQ ID NO:52), hsFATP5 (SEQ ID NO:54) or hsFATP6 (SEQ ID NO:56); 4.) a nucleotide sequence which consists of the coding 10 region of hsFATP1 (SEQ ID NO:46), the coding region of hsFATP2 (SEQ ID NO:48), the coding region of hsFATP3 (SEQ ID NO:101), the coding region of hsFATP4 (SEQ ID NO:52), the coding region of hsFATP5 (SEQ ID NO:54), or the coding region of hsFATP6 (SEQ ID NO:56).

The invention further relates to nucleic acids (nucleic acid molecules or 15 polynucleotides) having nucleotide sequences identical over their entire length to those shown in the figures, for instance Figures 44A-44C (SEQ ID NO:46), Figures 46A and 46B (SEQ ID NO:48), Figures 94A and 94B (SEQ ID NO:101), Figures 50A-50C (SEQ ID NO:52), Figure 52 (SEQ ID NO:54), and Figures 54A-54C (SEQ ID NO:56). It further relates to DNA, which due to the degeneracy of the genetic code, encodes a 20 FATP encoded by one of the FATP-encoding DNAs, whose amino acid sequence is provided herein. Also provided by the invention are nucleic acids having the coding sequences for the mature polypeptides or fragments in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or prepro- protein sequence. The nucleic acids of the invention encompass nucleic acids 25 that include a single continuous region or discontinuous regions encoding the polypeptide, together with additional regions, that may also contain coding or non-coding sequences. The nucleic acids may also contain non-coding sequences, including, for example, but not limited to, non-coding 5' and 3' sequences, such as the transcribed, non-translated sequences, termination signals, ribosome binding sites, sequences that

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stabilize mRNA, introns, polyadenylation signals, and additional coding sequences which encode additional amino acids. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain embodiments of the invention, the marker sequence can be a hexa-histidine peptide, as provided in the pQE
5 vector (Qiagen, Inc.) and described in Gentz *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 821-824 (1989), or an HA tag (Wilson *et al.*, *Cell* 37: 767 (1984)), or a sequence encoding glutathione S-transferase of *Schistosoma japonicum* (vectors available from Pharmacia; see Smith, D.B. and Johnson K.S., *Gene* 67:31 (1988) and Kaelin, W.G. *et al.*, *Cell* 70:351 (1992)). Nucleic acids of the invention also include, but are not limited to,
10 nucleic acids comprising a structural gene and its naturally associated sequences that control gene expression.

The invention further relates to variants, including naturally-occurring allelic variants, of those nucleic acids described specifically herein by DNA sequence, that encode variants of such polypeptides as those having the amino acid sequences shown
15 in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figures 94A and 94B (SEQ ID NO:102), Figure 51 (SEQ ID NO:53) Figure 53 (SEQ ID NO:55), or Figure 55 (SEQ ID NO:57). Such variants include nucleic acids encoding variants of the above-listed amino acid sequences, wherein those variants have several, such as 5 to 10, 1 to 5, or 3, 2 or 1 amino acids substituted, deleted, or added, in any combination. Variants include
20 polynucleotides encoding polypeptides with at least 95% but less than 100% amino acid sequence identity to the polypeptides described herein by amino acid sequence. Variant polynucleotides hybridize, under low to high stringency conditions, to the alleles described herein by DNA sequence. In one embodiment, variants have silent substitutions, additions and deletions that do not alter the properties and activities of the
25 FATP. Allelic variants of the polynucleotides encoding hsFATP1 (Figure 45; SEQ ID NO:47), hsFATP2 (Figure 47; SEQ ID NO:49), hsFATP3 (Figures 94A and 94B; SEQ ID NO:102), hsFATP4 (Figure 51; SEQ ID NO:53), Figure 53 (SEQ ID NO:55) and hsFATP6 (Figure 55; SEQ ID NO:57) will be identified as mapping to chromosomal locations listed for the corresponding wild type genes in Table 2 in Example 1.

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Orthologous genes are gene loci in different species that are sufficiently similar to each other in their nucleotide sequences to suggest that they originated from a common ancestral gene. Orthologous genes arise when a lineage splits into two species, rather than when a gene is duplicated within a genome. Proteins that are orthologs are encoded by genes of two different species, wherein the genes are said to be orthologous.

The invention further relates to polynucleotides encoding polypeptides which are orthologous to those polypeptides having a specific amino acid sequence described herein, such as the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figures 94A and 94B (SEQ ID NO:102), Figure 51 (SEQ ID NO:53), Figure 53 (SEQ ID NO:55), or Figure 55 (SEQ ID NO:57). These polynucleotides, which can be called ortholog polynucleotides, encode orthologous polypeptides that can range in amino acid sequence identity to a reference amino acid sequence described herein, from about 65% to less than 100%, but preferably 70% to 80%, more preferably 80% to 90%, and still more preferably 90% to less than 100%.

Orthologous polypeptides can also be those polypeptides that range in amino acid sequence similarity to a reference amino acid sequence described herein from about 75% to 100%, within the signature sequence. The amino acid sequence similarity between the signature sequences of orthologous polypeptides is preferably 80%, more preferably 90%, and still more preferably, 95%. The ortholog polynucleotides encode polypeptides that have similar functional characteristics (e.g., fatty acid transport activity) and similar tissue distribution, as appropriate to the organism from which the ortholog polynucleotides can be isolated.

Ortholog polynucleotides can be isolated from (e.g., by cloning or nucleic acid amplification methods) a great number of species, as shown by the sample of FATPs from evolutionarily divergent species described herein (see, e.g., Figures 44A-C through Figure 89). Ortholog polynucleotides corresponding to those in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figures 94A and 94B (SEQ ID NO:101), Figure 51 (SEQ ID NO:53), Figure 52 (SEQ ID NO:54) and Figure 55 (SEQ ID NO:57) are

those which can be isolated from mammals such as rat, dog, chimpanzee, monkey, baboon, pig, rabbit and guinea pig, for example.

Further variants that are fragments of the nucleic acids of the invention may be used to synthesize full-length nucleic acids of the invention, such as by use as primers in a polymerase chain reaction. As used herein, the term primer refers to a single-stranded oligonucleotide which acts as a point of initiation of template-directed DNA synthesis under appropriate conditions (e.g., in the presence of four different nucleoside triphosphates and an agent for polymerization, such as DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30 nucleotides. Short primer molecules generally require cooler temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template, but must be sufficiently complementary to hybridize with a template. The term primer site refers to the area of the target DNA to which a primer hybridizes. The term primer pair refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

Further embodiments of the invention are nucleic acids that are at least 80% identical over their entire length to a nucleic acid described herein, for example a nucleic acid having the nucleotide sequence in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figures 94A and 94B (SEQ ID NO:101), Figures 50A-50C (SEQ ID NO:52), Figure 52 (SEQ ID NO:54), and Figures 54A-54C (SEQ ID NO:56). Additional embodiments are nucleic acids, and the complements of such nucleic acids, having at least 90% nucleotide sequence identity to the above-described sequences, and nucleic acids having at least 95% nucleotide sequence identity. In preferred embodiments, DNA of the present invention has 97% nucleotide sequence identity, 98% nucleotide sequence identity, or at least 99% nucleotide sequence identity with the DNA whose sequences are presented herein.

Other embodiments of the invention are nucleic acids that are at least 80% identical in nucleotide sequence to a nucleic acid encoding a polypeptide having an amino acid sequence as set forth in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figures 94A and 94B (SEQ ID NO:102), Figure 51 (SEQ ID NO:53), Figure 53 (SEQ ID NO:55) or Figure 55 (SEQ ID NO:57), or as such amino acid sequences are set forth elsewhere herein, and nucleic acids that are complementary to such nucleic acids. Specific embodiments are nucleic acids having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide having an amino acid sequence as described in the list above, nucleic acids having at least 95% sequence identity, and nucleic acids having at least 97% sequence identity.

The terms "complementary" or "complementarity" as used herein, refer to the natural binding of polynucleotides under permissive salt and temperature conditions by base-pairing. Complementarity between two single-stranded molecules may be "partial" in which only some of the nucleic acids bind, or it may be complete when total complementarity exists between the single-stranded molecules (that is, when A-T and G-C base pairing is 100% complete). The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands. This is of particular importance in amplification reactions, which depend on binding between nucleic acid strands.

The invention further includes nucleic acids that hybridize to the above-described nucleic acids, especially those nucleic acids that hybridize under stringent hybridization conditions. "Stringent hybridization conditions" or "high stringency conditions" generally occur within a range from about T_m minus 5°C (5° C below the strand dissociation temperature or melting temperature (T_m) of the probe nucleic acid molecule) to about 20° C to 25° C below T_m . As will be understood by those of skill in the art, the stringency of hybridization may be altered in order to identify or detect molecules having identical or related polynucleotide sequences. An example of high stringency hybridization follows. Hybridization solution is (6x SSC/10 mM EDTA/0.5% SDS/5x Denhardt's solution/100 µg/ml sheared and denatured salmon

sperm DNA). Hybridization is at 64-65°C for 16 hours. The hybridized blot is washed two times with 2x SSC/0.5% SDS solution at room temperature for 15 minutes each, and two times with 0.2x SSC/0.5% SDS at 65°C, for one hour each. Further examples of high stringency conditions can be found on pages 2.10.1-2.10.16 (see particularly 2.10.8-11) and pages 6.3.1-6 in *Current Protocols in Molecular Biology* (Ausubel, F.M. *et al.*, eds., containing supplements up through Supplement 42, 1998). Examples of high, medium, and low stringency conditions can be found on pages 36 and 37 of WO 98/40404, which are incorporated herein by reference.

The invention further relates to nucleic acids obtainable by screening an appropriate library with a probe having a nucleotide sequence such as that set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figures 94A and 94B (SEQ ID NO:101), Figures 50A-50C (SEQ ID NO:52), Figure 52 (SEQ ID NO:54) or Figures 54A-54C (SEQ ID NO:56), or a probe which is a sufficiently long fragment of any of the above; and isolating the nucleic acid. Such probes generally can comprise at least 15 nucleotides. Nucleic acids obtainable by such screenings may include RNAs, cDNAs and genomic DNA, for example, encoding FATPs of the FATP family described herein.

Further uses for the nucleic acid molecules of the invention, whether encoding a full-length FATP or whether comprising a contiguous portion of a nucleic acid molecule such as one given in SEQ ID NO:46, 48, 101, 52, 54, or 56, include use as markers for tissues in which the corresponding protein is preferentially expressed (to identify constitutively expressed proteins or proteins produced at a particular stage of tissue differentiation or stage of development of a disease state); as molecular weight markers on southern gels; as chromosome markers or tags (when labeled, for example with biotin, a radioactive label or a fluorescent label) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in a mammal to identify potential genetic disorders; as probes to hybridize and thus identify, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of

discovering other novel nucleic acid molecules; for selecting and making oligomers for attachment to a "gene chip" or other support, to be used, for example, for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or to elicit another immune response.

Further methods to obtain nucleic acids encoding FATPs of the FATP family include PCR and variations thereof (e.g., "RACE" PCR and semi-specific PCR methods). Portions of the nucleic acids having a nucleotide sequence set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figures 94A and 94B (SEQ ID NO:101), Figures 50A-50C (SEQ ID NO:52), Figure 52 (SEQ ID NO:54) or Figures 54A-54C (SEQ ID NO:56), (especially "flanking sequences" on either side of a coding region) can be used as primers in methods using the polymerase chain reaction, to produce DNA from an appropriate template nucleic acid.

Once a fragment of the FATP gene is generated by PCR, it can be sequenced, and the sequence of the product can be compared to other DNA sequences, for example, by using the BLAST Network Service at the National Center for Biotechnology Information. The boundaries of the open reading frame can then be identified using semi-specific PCR or other suitable methods such as library screening. Once the 5' initiator methionine codon and the 3' stop codon have been identified, a PCR product encoding the full-length gene can be generated using genomic DNA as a template, with primers complementary to the extreme 5' and 3' ends of the gene or to their flanking sequences. The full-length genes can then be cloned into expression vectors for the production of functional proteins.

The invention also relates to isolated proteins or polypeptides such as those encoded by nucleic acids of the present invention. Isolated proteins can be purified from a natural source or can be made recombinantly. Proteins or polypeptides referred to herein as "isolated" are proteins or polypeptides that exist in a state different from the state in which they exist in cells in which they are normally expressed in an organism, and include proteins or polypeptides obtained by methods described herein, similar

state in which they exist in cells in which they are normally expressed in an organism, and include proteins or polypeptides obtained by methods described herein, similar methods or other suitable methods, and also include essentially pure proteins or polypeptides, proteins or polypeptides produced by chemical synthesis or by combinations of biological and chemical methods, and recombinant proteins or polypeptides which are isolated. Thus, the term "isolated" as used herein, indicates that the polypeptide in question exists in a physical milieu distinct from that in which it occurs in nature. Thus, "isolated" includes existing in membrane fragments and vesicles membrane fractions, liposomes, lipid bilayers and other artificial membrane systems.

10 An isolated FATP may be substantially isolated with respect to the complex cellular milieu in which it naturally occurs, and may even be purified essentially to homogeneity, for example as determined by PAGE or column chromatography (for example, HPLC), but may also have further cofactors or molecular stabilizers, such as detergents, added to the purified protein to enhance activity. In one embodiment, proteins or polypeptides are isolated to a state at least about 75% pure; more preferably at least about 85% pure, and still more preferably at least about 95% pure, as determined by Coomassie blue staining of proteins on SDS-polyacrylamide gels. Proteins or polypeptides referred to herein as "recombinant" are proteins or polypeptides produced by the expression of recombinant nucleic acids.

20 In a preferred embodiment, an isolated polypeptide comprising a FATP, a functional portion thereof, or a functional equivalent of the FATP, has at least one function characteristic of a FATP, for example, transport activity, binding function (e.g., a domain which binds to AMP), or antigenic function (e.g., binding of antibodies that also bind to a naturally-occurring FATP, as that function is found in an antigenic determinant). Functional equivalents can have activities that are quantitatively similar to, greater than, or less than, the reference protein. These proteins include, for example, naturally occurring FATPs that can be purified from tissues in which they are produced (including polymorphic or allelic variants), variants (e.g., mutants) of those proteins and/or portions thereof. Such variants include mutants differing by the addition,

deletion or substitution of one or more amino acid residues, or modified polypeptides in which one or more residues are modified, and mutants comprising one or more modified residues. Portions or fragments of a FATP can range in size from four amino acid residues to the entire amino acid sequence minus one amino acid.

5 The isolated proteins of the invention preferably include mammalian fatty acid transport proteins of the FATP family of homologous proteins. In one embodiment, the extent of amino acid sequence similarity between a polypeptide having one of the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figures 94A and 94B (SEQ ID NO:102), Figure 51 (SEQ ID NO:53), Figure 53 (SEQ
10 ID NO:55), or Figure 55 (SEQ ID NO:57), and the respective functional equivalents of these polypeptides is at least about 88%. In other embodiments, the degree of amino acid sequence similarity between a FATP and its respective functional equivalent is at least about 91%, at least about 94%, or at least about 97%.

 The polypeptides of the invention also include those FATPs encoded by
15 polynucleotides which are orthologous to those polynucleotides, the sequences of which are described herein in whole or in part. FATPs which are orthologs to those described herein by amino acid sequence, in whole or in part, are, for example fatty acid transport proteins 1-6 of dog, rat chimpanzee, monkey, rabbit, guinea pig, baboon and pig, and are also embodiments of the invention.

20 To determine the percent identity or similarity of two amino acid sequences or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment, and non-homologous (dissimilar) sequences can be disregarded for comparison purposes). In a preferred embodiment, the
25 length of a reference sequence aligned for comparison purposes is at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, and even more preferably at least 70%, 80%, or 90% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first

SEQUENCE LISTING

sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein, amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "similarity"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

The invention also encompasses polypeptides having a lower degree of identity but having sufficient similarity so as to perform one or more of the same functions performed by the polypeptides described herein by amino acid sequence. Similarity for a polypeptide is determined by conserved amino acid substitution. Such substitutions are those that substitute a given amino acid in a polypeptide by another amino acid of like characteristics. Conservative substitutions are likely to be phenotypically silent. Typically seen as conservative substitutions are the replacements, one for another, among the aliphatic amino acids Ala, Val, Leu, and Ile; interchange of the hydroxyl residues Ser and Thr, exchange of the acidic residues Asp and Glu, substitution between the amide residues Asn and Gln, exchange of the basic residues Lys and Arg and replacements among the aromatic residues Phe, Tyr. Guidance concerning which amino acid changes are likely to be phenotypically silent is found in Bowie *et al.*, *Science* 247:1306-1310 (1990).

Sequence 10590460

TABLE 1. Conservative Amino Acid Substitutions

Aromatic		Phenylalanine	
		Tryptophan	
		Tyrosine	
Hydrophobic		Leucine	
		Isoleucine	
		Valine	
Polar		Glutamine	
		Asparagine	
Basic		Arginine	
		Lysine	
		Histidine	
Acidic		Aspartic Acid	
		Glutamic Acid	
Small		Alanine	
		Serine	
		Threonine	
		Methionine	
		Glycine	

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm.

10 (Computational Molecular Biology, Lesk, A.M.,ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence

Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereaux, J., eds., M. Stockton

Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.*

- 5 (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the
- 10 GCG software package (Devereux, J., *et al.*, *Nucleic Acids Res.* 12(1):387 (1984)) (available at <http://www.gcg.com>), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (*CABIOS*, 4:11-17 (1989))
- 15 which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against databases to, for example,

identify other family members or related sequences. Such searches can be performed

- 20 using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (*J. Mol. Biol.* 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, word length = 12 to obtain nucleotide sequences homologous to (with calculatably significant similarity to) the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program,
- 25 score = 50, word length = 3 to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (*Nucleic Acids Res.* 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default

parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

Similarity for nucleotide and amino acid sequences can be defined in terms of the parameters set by the Advanced Blast search available from NCBI (the National Center for Biotechnology Information; see, for Advanced BLAST page, www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=1). These default parameters, recommended for a query molecule of length greater than 85 amino acid residues or nucleotides have been set as follows: gap existence cost, 11, per residue gap cost, 1; lambda ratio, 0.85. Further explanation of version 2.0 of BLAST can be found on related website pages and in Altschul, S.F. *et al.*, *Nucleic Acids Res.* 25:3389-3402 (1997).

The invention further relates to fusion proteins, comprising a FATP or functional portion thereof (as described above) as a first moiety, linked to second moiety not occurring in the FATP as found in nature. Thus, the second moiety can be an amino acid, peptide or polypeptide. The first moiety can be in an N-terminal location, C-terminal location or internal to the fusion protein. In one embodiment, the fusion protein comprises a FATP as the first moiety, and a second moiety comprising a linker sequence and an affinity ligand. Fusion proteins can be produced by a variety of methods. For example, a fusion protein can be produced by the insertion of a FATP gene or portion thereof into a suitable expression vector, such as Bluescript SK +/- (Stratagene), pGEX-4T-2 (Pharmacia), pET-24(+) (Novagen), or vectors of similar construction. The resulting construct can be introduced into a suitable host cell for expression. Upon expression, fusion protein can be purified from cells by means of a suitable affinity matrix (See e.g., *Current Protocols in Molecular Biology*, Ausubel, F.M. *et al.*, eds., Vol. 2, pp. 16.4.1-16.7.8, containing supplements up through Supplement 42, 1998).

The invention also relates to enzymatically produced, synthetically produced, or recombinantly produced portions of a fatty acid transport protein. Portions of a FATP can be made which have full or partial function on their own, or which when mixed

together (though fully, partially, or nonfunctional alone), spontaneously assemble with one or more other polypeptides to reconstitute a functional protein having at least one function characteristic of a FATP.

Fragments of a FATP can be produced by direct peptide synthesis, for example
5 those using solid-phase techniques (Roberge, J.Y. *et al.*, *Science* 269:202-204 (1995); Merrifield, J., *J. Am. Chem. Soc.* 85:2149-2154 (1963)). Protein synthesis can be performed using manual techniques or by automation. Automated synthesis can be carried out using, for instance, an Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Various fragments of a FATP can be synthesized separately and
10 combined using chemical methods.

One aspect of the invention is a peptide or polypeptide having the amino acid sequence of a portion of a fatty acid transport protein which is hydrophilic rather than hydrophobic, and ordinarily can be detected as facing the outside of the cell membrane. Such a peptide or polypeptide can be thought of as being an extracellular domain of the
15 FATP, or a mimetic of said extracellular domain. It is known, for example, that a portion of human FATP4 that includes a highly conserved motif is involved in AMP-CoA binding function (Stuhlsatz-Krouper, S.M. *et al.*, *J. Biol. Chem.* 44:28642-28650 (1998)).

The term "mimetic" as used herein, refers to a molecule, the structure of which
20 is developed from knowledge of the structure of the FATP of interest, or one or more portions thereof, and, as such, is able to effect some or all of the functions of a FATP.

Portions of an FATP can be prepared by enzymatic cleavage of the isolated protein, or can be made by chemical synthesis methods. Portions of a FATP can also be made by recombinant DNA methods in which restriction fragments, or fragments that
25 may have undergone further enzymatic processing, or synthetically made DNAs are joined together to construct an altered FATP gene. The gene can be made such that it encodes one or more desired portions of a FATP. These portions of FATP can be entirely homologous to a known FATP, or can be altered in amino acid sequence relative to naturally occurring FATPs to enhance or introduce desired properties such as

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solubility, stability, or affinity to a ligand. A further feature of the gene can be a sequence encoding an N-terminal signal peptide directed to the plasma membrane.

An extracellular domain can be determined by a hydrophobicity plot, such as those shown in Figures 28A, 29A, and 35A, or by a hydrophilicity plot such as those shown in Figures 28C, 29C, 35C, 91, 92 and 93. A polypeptide or peptide comprising all or a portion of a FATP extracellular domain can be used in a pharmaceutical composition. When administered to a mammal by an appropriate route, the polypeptide or peptide can bind to fatty acids and compete with the native FATPs in the membrane of cells, thereby making fewer fatty acid molecules available as substrates for transport into cells, and reducing the amount of fatty acids taken up by, for example, the heart, in the case of FATP6.

Another aspect of the invention relates to a method of producing a fatty acid transport protein, variants or portions thereof, and to expression systems and host cells containing a vector appropriate for expression of a fatty acid transport protein.

Cells that express a FATP, a variant or a portion thereof, or an ortholog of a FATP described herein by amino acid sequence, can be made and maintained in culture, under conditions suitable for expression, to produce protein in the cells for cell-based assays, or to produce protein for isolation. These cells can be procaryotic or eucaryotic. Examples of procaryotic cells that can be used for expression include *Escherichia coli*, *Bacillus subtilis* and other bacteria. Examples of eucaryotic cells that can be used for expression include yeasts such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Pichia pastoris* and other lower eucaryotic cells, and cells of higher eucaryotes such as those from insects and mammals, such as primary cells and cell lines such as CHO, HeLa, 3T3 and BHK cells, preferably COS cells and human kidney 293 cells, and more preferably Jurkat cells. (See, e.g., Ausubel, F.M. *et al.*, eds. *Current Protocols in Molecular Biology*, Greene Publishing Associates and John Wiley & Sons, Inc., containing Supplements up through Supplement 42, 1998)).

In one embodiment, host cells that produce a recombinant FATP, or a portion thereof, a variant, or an ortholog of a FATP described herein by amino acid sequence,

can be made as follows. A gene encoding a FATP, variant or a portion thereof can be inserted into a nucleic acid vector, e.g., a DNA vector, such as a plasmid, phage, cosmid, phagemid, virus, virus-derived vector (e.g., SV40, vaccinia, adenovirus, fowl pox virus, pseudorabies viruses, retroviruses) or other suitable replicon, which can be present in a single copy or multiple copies, or the gene can be integrated in a host cell chromosome. A suitable replicon or integrated gene can contain all or part of the coding sequence for a FATP or variant, operably linked to one or more expression control regions whereby the coding sequence is under the control of transcription signals and linked to appropriate translation signals to permit translation. The vector can be introduced into cells by a method appropriate to the type of host cells (e.g., transfection, electroporation, infection). For expression from the FATP gene, the host cells can be maintained under appropriate conditions (e.g., in the presence of inducer, normal growth conditions, etc.). Proteins or polypeptides thus produced can be recovered (e.g., from the cells, as in a membrane fraction, from the periplasmic space of bacteria, from culture medium) using suitable techniques. Appropriate membrane targeting signals may be incorporated into the expressed polypeptide. These signals may be endogenous to the polypeptide or they may be heterologous signals.

Polypeptides of the invention can be recovered and purified from cell cultures (or from their primary cell source) by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and high performance liquid chromatography. Known methods for refolding protein can be used to regenerate active conformation if the polypeptide is denatured during isolation or purification.

In a further aspect of the invention are methods for assessing the transport function of any of the fatty acid transport proteins or polypeptides described herein, including orthologs, and in variations of these, methods for identifying an inhibitor (or an enhancer) of such function and methods for assessing the transport function in the presence of a candidate inhibitor or a known inhibitor.

A variety of systems comprising living cells can be used for these methods. Cells to be used in fatty acid transport assays, and further in methods for identifying an inhibitor or enhancer of this function, express one or more FATPs. See Examples 3, 6, 9, 12 and 14 for data on tissue distribution of expression of FATPs, and Examples 10 and 11 describing recombinant cells expressing FATP. Cells for use in cell-based assays described herein can be drawn from a variety of sources, such as isolated primary cells of various organs and tissues wherein one or more FATPs are naturally expressed. In some cases, the cells can be from adult organs, and in some cases, from embryonic or fetal organs, such as heart, lung, liver, intestine, skeletal muscle, kidney and the like.

Cells for this purpose can also include cells cultured as fragments of organs or in conditions simulating the cell type and/or tissue organization of organs, in which artificial materials may be used as substrates for cell growth. Other types of cells suitable for this purpose include cells of a cell strain or cell line (ordinarily comprising cells considered to be "transformed") transfected to express one or more FATPs.

A further embodiment of the invention is a method for detecting, in a sample of cells, a fatty acid transport protein, a portion or fragment thereof, a fusion protein comprising a FATP or a portion thereof, or an ortholog as described herein, wherein the cells can be, for instance, cells of a tissue, primary culture cells, or cells of a cell line, including cells into which nucleic acid has been introduced. The method comprises adding to the sample an agent that specifically binds to the protein, and detecting the agent specifically bound to the protein. Appropriate washing steps can be added to reduce nonspecific binding to the agent. The agent can be, for example, an antibody, a ligand or a substrate mimic. The agent can have incorporated into it, or have bound to it, covalently or by high affinity non-covalent interactions, for instance, a label that facilitates detection of the agent to which it is bound, wherein the label can be, but is not limited to, a phosphorescent label, a fluorescent label, a biotin or avidin label, or a radioactive label. The means of detection of a fatty acid transport protein can vary, as appropriate to the agent and label used. For example, for an antibody that binds to the fatty acid transport protein, the means of detection may call for binding a second

antibody, which has been conjugated to an enzyme, to the antibody which binds the fatty acid transport protein, and detecting the presence of the second antibody by means of the enzymatic activity of the conjugated enzyme.

Similar principles can also be applied to a cell lysate or a more purified
5 preparation of proteins from cells that may comprise a fatty acid transport protein of interest, for example in the methods of immunoprecipitation, immunoblotting, immunoaffinity methods, that in addition to detection of the particular FATP, can also be used in purification steps, and qualitative and quantitative immunoassays. See, for instance, chapters 11 through 14 in *Antibodies: A Laboratory Manual*, E. Harlow and
10 D. Lane, eds., Cold Spring Harbor Laboratory, 1988.

Isolated fatty acid transport protein or, an antigenically similar portion thereof, especially a portion that is soluble, can be used in a method to select and identify molecules which bind specifically to the FATP. Fusion proteins comprising all of, or a portion of, the fatty acid transport protein linked to a second moiety not occurring in the
15 FATP as found in nature, can be prepared for use in another embodiment of the method. Suitable fusion proteins for this purpose include those in which the second moiety comprises an affinity ligand (e.g., an enzyme, antigen, epitope). FATP fusion proteins can be produced by the insertion of a gene encoding the FATP or a variant thereof, or a suitable portion of such gene into a suitable expression vector, which encodes an
20 affinity ligand (e.g., pGEX-4T-2 and pET-15b, encoding glutathione S-transferase and His-Tag affinity ligands, respectively). The expression vector can be introduced into a suitable host cell for expression. Host cells are lysed and the lysate, containing fusion protein, can be bound to a suitable affinity matrix by contacting the lysate with an affinity matrix.

25 In one embodiment, the fusion protein can be immobilized on a suitable affinity matrix under conditions sufficient to bind the affinity ligand portion of the fusion protein to the matrix, and is contacted with one or more candidate binding agents (e.g., a mixture of peptides) to be tested, under conditions suitable for binding of the binding agents to the FATP portion of the bound fusion protein. Next, the affinity matrix with

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bound fusion protein can be washed with a suitable wash buffer to remove unbound candidate binding agents and non-specifically bound candidate binding agents. Those agents which remain bound can be released by contacting the affinity matrix with fusion protein bound thereto with a suitable elution buffer. Wash buffer can be formulated to
5 permit binding of the fusion protein to the affinity matrix, without significantly disrupting binding of specifically bound binding agents. In this aspect, elution buffer can be formulated to permit retention of the fusion protein by the affinity matrix, but can be formulated to interfere with binding of the candidate binding agents to the target portion of the fusion protein. For example, a change in the ionic strength or pH of the
10 elution buffer can lead to release of specifically bound agent, or the elution buffer can comprise a release component or components designed to disrupt binding of specifically bound agent to the target portion of the fusion protein.

Immobilization can be performed prior to, simultaneous with, or after, contacting the fusion protein with candidate binding agent, as appropriate. Various
15 permutations of the method are possible, depending upon factors such as the candidate molecules tested, the affinity matrix-ligand pair selected, and elution buffer formulation. For example, after the wash step, fusion protein with binding agent molecules bound thereto can be eluted from the affinity matrix with a suitable elution buffer (a matrix elution buffer, such as glutathione for a GST fusion). Where the fusion protein
20 comprises a cleavable linker, such as a thrombin cleavage site, cleavage from the affinity ligand can release a portion of the fusion with the candidate agent bound thereto. Bound agent molecules can then be released from the fusion protein or its cleavage product by an appropriate method, such as extraction.

One or more candidate binding agents can be tested simultaneously. Where a
25 mixture of candidate binding agents is tested, those found to bind by the foregoing processes can be separated (as appropriate) and identified by suitable methods (e.g., PCR, sequencing, chromatography). Large libraries of candidate binding agents (e.g., peptides, RNA oligonucleotides) produced by combinatorial chemical synthesis or by other methods can be tested (see e.g., Ohlmeyer, M.H.J. *et al.*, *Proc. Natl. Acad. Sci.*

USA 90:10922-10926 (1993) and DeWitt, S.H. *et al.*, *Proc. Natl. Acad. Sci. USA* 90:6909-6913 (1993), relating to tagged compounds; see also Rutter, W.J. *et al.* U.S. Patent No. 5,010,175; Huebner, V.D. *et al.*, U.S. Patent No. 5,182,366; and Geysen, H.M., U.S. Patent No. 4,833,092). Random sequence RNA libraries (see Ellington, A.D. *et al.*, *Nature* 346:818-822 (1990); Bock, L.C. *et al.*, *Nature* 355:584-566 (1992); and Szostak, J.W., *Trends in Biochem. Sci.* 17:89-93 (March, 1992)) can also be screened according to the present method to select RNA molecules which bind to a target FATP or FATP fusion protein. Where binding agents selected from a combinatorial library by the present method carry unique tags, identification of individual biomolecules by chromatographic methods is possible. Where binding agents do not carry tags, chromatographic separation, followed by mass spectrometry to ascertain structure, can be used to identify binding agents selected by the method, for example.

The invention also comprises a method for identifying an agent which inhibits interaction between a fatty acid transport protein (e.g., one comprising the amino acid sequence in SEQ ID NO:47, SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID NO:102, or SEQ ID NO:57), and a ligand of said protein. The FATP can be one described by amino acid sequence herein, a portion or fragment thereof, a variant thereof, or an ortholog thereof, or a FATP fusion protein. Here, a ligand can be, for instance, a substrate, or a substrate mimic, an antibody, or a compound, such as a peptide, that binds with specificity to a site on the protein. The method comprises combining, not limited to a particular order, the fatty acid protein, the ligand of the protein, and a candidate agent to be assessed for its ability to inhibit interaction between the protein and the ligand, under conditions appropriate for interaction between the protein and the ligand (e.g., pH, salt, temperature conditions conducive to appropriate conformation and molecular interactions); determining the extent to which the protein and ligand interact; and comparing (1) the extent of protein-ligand interaction in the presence of candidate agent with (2) the extent of protein-ligand interaction in the

absence of candidate agent, wherein if (1) is less than (2), then the candidate agent is one which inhibits interaction between the protein and the ligand.

The method can be facilitated, for example, by using an experimental system which employs a solid support (column chromatography matrix, wall of a plate,

- 5 microtiter wells, column pore glass, pins to be submerged in a solution, beads, etc.) to which the protein can be attached. Accordingly, in one embodiment, the protein can be fixed to a solid phase directly or indirectly, by a linker. The candidate agent to be tested is added under conditions conducive for interaction and binding to the protein. The ligand is added to the solid phase system under conditions appropriate for binding.
- 10 Excess ligand is removed, as by a series of washes done under conditions that do not disrupt protein-ligand interactions. Detection of bound ligand can be facilitated by using a ligand that carries a label (e.g., fluorescent, chemiluminescent, radioactive). In a control experiment, protein and ligand are allowed to interact in the absence of any candidate agent, under conditions otherwise identical to those used for the "test"
- 15 conditions where candidate inhibiting agent is present, and any washes used in the test conditions are also used in the control. The extent to which ligand binds to the protein in the presence of candidate agent is compared to the extent to which ligand binds to the protein in the absence of the candidate agent. If the extent to which interaction of the protein and the ligand occurs is less in the presence of the candidate agent than in the
- 20 absence of the candidate agent, the candidate agent is an agent which inhibits interaction between the protein and the ligand of the protein.

In a further embodiment, an inhibitor (or an enhancer) of a fatty acid transport protein can be identified. The method comprises steps which are, or are variations of the following: contacting the cells with fatty acid, wherein the fatty acid can be labeled

25 for convenience of detection; contacting a first aliquot of the cells with an agent being tested as an inhibitor (or enhancer) of fatty acid uptake while maintaining a second aliquot of cells under the same conditions but without contact with the agent; and measuring (e.g., quantitating) fatty acid in the first and second aliquots of cells; wherein a lesser quantity of fatty acid in the first aliquot compared to that in the second aliquot

is indicative that the agent is an inhibitor of fatty acid uptake by a fatty acid transport protein. A greater quantity of fatty acid in the first aliquot compared to that in the second aliquot is indicative that the agent is an enhancer of fatty acid uptake by a fatty acid transport protein.

- 5 A particular embodiment of identifying an inhibitor or enhancer of fatty acid transport function employs the above steps, but also employs additional steps preceding those given above: introducing into cells of a cell strain or cell line ("host cells" for the intended introduction of, or after the introduction of, a vector) a vector comprising a fatty acid transport protein gene, wherein expression of the gene can be regulatable or
- 10 constitutive, and providing conditions to the host cells under which expression of the gene can occur.

- The terms "contacting" and "combining" as used herein in the context of bringing molecules into close proximity to each other, can be accomplished by conventional means. For example, when referring to molecules that are soluble,
- 15 contacting is achieved by adding the molecules together in a solution. "Contacting" can also be adding an agent to a test system, such as a vessel containing cells in tissue culture.

- The term "inhibitor" or "antagonist", as used herein, refers to an agent which blocks, diminishes, inhibits, hinders, limits, decreases, reduces, restricts or interferes
- 20 with fatty acid transport into the cytoplasm of a cell, or alternatively and additionally, prevents or impedes the cellular effects associated with fatty acid transport. The term "enhancer" or "agonist", as used herein, refers to an agent which augments, enhances, or increases fatty acid transport into the cytoplasm of a cell. An antagonist will decrease fatty acid concentration, fatty acid metabolism and byproduct levels in the cell, leading
- 25 to phenotypic and molecular changes.

In order to produce a "host cell" type suitable for fatty acid uptake assays and for assays derived therefrom for identifying inhibitors or enhancers thereof, a nucleic acid vector can be constructed to comprise a gene encoding a fatty acid transport protein, for example, human FATP1, FATP2, FATP3, FATP4, FATP5, FATP6, a mutant or variant

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thereof, an ortholog of the human proteins, such as mouse orthologs or orthologs found in other mammals, or a FATP family protein of origin in an organism other than a mammal. The gene of the vector can be regulatable, such as by the placement of the gene under the control of an inducible or repressible promoter in the vector (e.g., inducible or repressible by a change in growth conditions of the host cell harboring the vector, such as addition of inducer, binding or functional removal of repressor from the cell milieu, or change in temperature) such that expression of the FATP gene can be turned on or initiated by causing a change in growth conditions, thereby causing the protein encoded by the gene to be produced, in host cells comprising the vector, as a plasma membrane protein. Alternatively, the FATP gene can be constitutively expressed.

A vector comprising an FATP gene, such as a vector described herein, can be introduced into host cells by a means appropriate to the vector and to the host cell type. For example, commonly used methods such as electroporation, transfection, for instance, transfection using CaCl_2 , and transduction (as for a virus or bacteriophage) can be used. Host cells can be, for example, mammalian cells such as primary culture cells or cells of cell lines such as COS cells, 293 cells or Jurkat cells. Host cells can also be, in some cases, cells derived from insects, cells of insect cell lines, bacterial cells, such as *E. coli*, or yeast cells, such as *S. cerevisiae*. It is preferred that the fatty acid transport protein whose function is to be assessed, with or without a candidate inhibitor or enhancer, be produced in host cells whose ancestor cells originated in a species related to the species of origin of the FATP gene encoding the fatty acid transport protein. For example, it is preferable that tests of function or of inhibition or enhancement of a mammalian FATP be carried out in host mammalian cells producing the FATP, rather than bacterial cells or yeast cells.

Host cells comprising a vector comprising a regulatable FATP gene can be treated so as to allow expression of the FATP gene and production of the encoded protein (e.g., by contacting the cells with an inducer compound that effects transcription from an inducible promoter operably linked to the FATP gene).

The test agent (e.g., an agonist or antagonist) is added to the cells to be used in a fatty acid transport assay, in the presence or absence of test agent, under conditions suitable for production and/or maintenance of the expressed FATP in a conformation appropriate for association of the FATP with test agent and substrate. For example, conditions under which an agent is assessed, such as media and temperature requirements, can, initially, be similar to those necessary for transport of typical fatty acid substrates across the plasma membrane. One of ordinary skill in the art will know how to vary experimental conditions depending upon the biochemical nature of the test agent. The test agent can be added to the cells in the presence of fatty acid, or in the absence of fatty acid substrate, with the fatty acid substrate being added following the addition of the test agent. The concentration at which the test agent can be evaluated can be varied, as appropriate, to test for an increased effect with increasing concentrations.

Test agents to be assessed for their effects on fatty acid transport can be any chemical (element, molecule, compound), made synthetically, made by recombinant techniques or isolated from a natural source. For example, test agents can be peptides, polypeptides, peptoids, sugars, hormones, or nucleic acid molecules, such as antisense nucleic acid molecules. In addition, test agents can be small molecules or molecules of greater complexity made by combinatorial chemistry, for example, and compiled into libraries. These libraries can comprise, for example, alcohols, alkyl halides, amines, amides, esters, aldehydes, ethers and other classes of organic compounds. Test agents can also be natural or genetically engineered products isolated from lysates of cells, bacterial, animal or plant, or can be the cell lysates themselves. Presentation of test compounds to the test system can be in either an isolated form or as mixtures of compounds, especially in initial screening steps.

Thus, the invention relates to a method for identifying agents which alter fatty acid transport, the method comprising providing the test agent to the cell (wherein "cell" includes the plural, and can include cells of a cell strain, cell line or culture of primary cells or organ culture, for example), under conditions suitable for binding to its target,

whether to the FATP itself or to another target on or in the cell, wherein the transformed cell comprises a FATP.

In greater detail, to test one or more agents or compounds (e.g., a mixture of compounds can conveniently be screened initially) for inhibition of the transport

5 function of a fatty acid transport protein, the agent(s) can be contacted with the cells.

The cells can be contacted with a labeled fatty acid. The fatty acid can be, for example, a known substrate of the fatty acid transport protein such as oleate or palmitate. The fatty acid can itself be labeled with a radioactive isotope, (e.g., ^3H or ^{14}C) or can have a radioactively labeled adduct attached. In other variations, the fatty acid can have

10 chemically attached to it a fluorescent label, or a substrate for an enzyme occurring within the cells, wherein the substrate yields a detectable product, such as a highly colored or fluorescent product. Addition of candidate inhibitors and labeled substrate to the cells comprising fatty acid transport protein can be in either order or can be simultaneous.

15 A second aliquot of cells, which can be called "control" cells (a "first" aliquot of cells can be called "test" cells), is treated, if necessary (as in the case of transformed "host" cells), so as to allow expression of the FATP gene, and is contacted with the labeled substrate of the fatty acid transport protein. The second aliquot of cells is not contacted with one or more agents to be tested for inhibition of the transport function of
20 the protein produced in the cells, but is otherwise kept under the same culture conditions as the first aliquot of cells.

In a further step of a method to identify inhibitors of a fatty acid transport protein, the labeled fatty acid is measured in the first and second aliquots of cells. A preliminary step of this measurement process can be to separate the external medium
25 from the cells so as to be able to distinguish the labeled fatty acid external to the cells from that which has been transported inside the cells. This can be accomplished, for instance, by removing the cells from their growth container, centrifuging the cell suspension, removing the supernatant and performing one or more wash steps to extensively dilute the remaining medium which may contain labeled fatty acid.

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Detection of the labeled fatty acid can be by a means appropriate to the label used. For example, for a radioactive label, detection can be by scintillation counting of appropriately prepared samples of cells (e.g., lysates or protein extracts); for a fluorescent label, by measuring fluorescence in the cells by appropriate instrumentation.

5 If a compound tested as a candidate inhibitor of transport function causes the test cells to have less labeled fatty acid detected in the cells than that detected in the control cells, then the compound is an inhibitor of the fatty acid transport protein. Procedures analogous to those above can be devised for identifying enhancers (agonists of FATPs) of fatty acid transport function wherein if the test cells contain more labeled fatty acid
10 than that detected in the control cells, or if the fatty acid is taken up at a higher rate, then the compound being tested can be concluded to be an enhancer of the fatty acid transport protein.

Example 13 describes use of an assay of this type to identify an inhibitor of a FATP. In Example 13, an antisense oligonucleotide which specifically inhibits biosynthesis of mmFATP4 was demonstrated to inhibit fatty acid uptake into mouse enterocytes. Similarly, antisense oligonucleotides directed towards specifically inhibiting the biosynthesis of FATP6 in heart cells, FATP5 in liver cells, FATP3 in lung cells, and FATP2 in colon cells, can be demonstrated as examples of "test agents" that inhibit fatty acid transport.

Another assay to determine whether an agent is an inhibitor (or enhancer) of fatty acid transport employs animals, one or more of which are administered the agent, and one or more of which are maintained under similar conditions, but are not administered the agent. Both groups of animals are given fatty acids (e.g., orally, intravenously, by tube inserted into stomach or intestine), and the fatty acids taken up into a bodily fluid (e.g., serum) or into an organ or tissue of interest are measured from comparable samples taken from each group of animals. The fatty acids may carry a label (e.g., radioactive) to facilitate detection and quantitation of fatty acids taken up into the fluid or tissue being sampled. This type of assay can be used alone or can be used in addition to *in vitro* assays of a candidate inhibitor or enhancer.

An agent determined to be an inhibitor (or enhancer) of FATP function, such as fatty acid binding and/or fatty acid uptake, can be administered to cells in culture, or *in vivo*, to a mammal (e.g. human) to inhibit (or enhance) FATP function. Such an agent may be one that acts directly on the FATP (for example, by binding) or can act on an intermediate in a biosynthetic pathway to produce FATP, such as transcription of the FATP gene, processing of the mRNA, or translation of the mRNA. An example of such an agent is antisense oligonucleotide.

Antisense methods similar to those illustrated in Example 13 can be used to determine the target FATP of a compound or agent that has an inhibitory or enhancing effect on fatty acid uptake. For example, antisense oligonucleotide directed to the inhibition of FATP4 biosynthesis can be added to lung cells or cell lines derived from lung cells. In addition, antisense oligonucleotides directed to the inhibition of other FATPs, except for FATP3, can also be added to the lung cells. The administration of antisense oligonucleotides in this manner ensures that the predominant FATP activity remaining in the cells comes from FATP3. After a period of incubation of the cells with the antisense oligonucleotides sufficient to deplete the plasma membrane of the FATPs whose biosynthesis has been inhibited, a test agent, preferably one that has been shown by some preliminary test to have an inhibitory or enhancing activity on fatty acid transport, can be added to the lung cells. If the test agent is now demonstrated, after treatment of the cells with antisense oligonucleotides, to have an inhibitory or enhancing activity on fatty acid transport in the lung cells, it can be concluded that the target of the test agent is FATP3, or a molecule involved in the biosynthesis or activity of FATP3.

In another type of cell-based assay for uptake of fatty acids, a change of intracellular pH resulting from the uptake of fatty acids can be followed by an indicator fluorophore. The fluorophore can be taken up by the cells in a preincubation step. Fatty acids can be added to the cell medium, and after some period of incubation to allow FATP-mediated uptake of fatty acids, the change in λ_{\max} of fluorescence can be measured, as an indicator of a change in intracellular pH, as the λ_{\max} of fluorescence of

the fluorophore changes with the pH of its environment, thereby indicating uptake of fatty acids. One such fluorophore is BCECF (2', 7'-bis(2-carboxyethyl)-5(6)-carboxyfluorescein; Rink, T.J. *et al.*, *J. Cell. Biol.* 95: 189 (1982)).

In assays similar to those described above, a candidate inhibitor or enhancer of fatty acid transport function can be added (or mock-added, for control cultures) to cultures of cells engineered to express a desired FATP to which fatty acid substrate is also added. Inhibition of fatty acid uptake is indicated by a lack of the drop in pH, indicating fatty acid uptake, that is seen in control cells. Enhancement of fatty acid uptake is indicated by a decrease in intracellular pH, as compared to control cells not receiving the candidate enhancer of fatty acid transport function.

Yeast cells can be used in a similar cell-based assay for the uptake of fatty acids mediated by a FATP, and such an assay can be adapted to a screening assay for the identification of agents that inhibit or enhance fatty acid uptake by an FATP. Yeast cells lacking an endogenous FATP activity (mutated, disrupted or deleted for *FAT1*; Faergeman, N.J. *et al.*, *J. Biol. Chem.* 272(13):8531-8538 (1997); Watkins, P.A. *et al.*, *J. Biol. Chem.* 273(29):18210-18219 (1998)) can be engineered to harbor a related gene of the family of FATP-encoding genes, such as a mammalian FATP (e.g., human FATP4).

Examples of expression vectors include pEG (Mitchell, D.A., *et al.*, *Yeast* 9:715-723 (1993)) and pDAD1 and pDAD2, which contain a *GAL1* promoter (Davis, L. I. and Fink, G. R., *Cell* 61:965-978 (1990)). A variety of promoters are suitable for expression. Available yeast vectors offer a choice of promoters. In one embodiment, the inducible *GAL1* promoter is used. In another embodiment, the constitutive *ADHI* promoter (alcohol dehydrogenase; Bennetzen, J. L. and Hall, B. D., *J. Biol. Chem.* 257:3026-3031 (1982)) can be used to express an inserted gene on glucose-containing media. An example of a vector suitable for expression of a heterologous FATP gene in yeast is pQB169.

With the introduced FATP gene providing the only fatty acid transport protein function for the yeast cells, it is possible to study effect of the heterologous FATP on

fatty acid transport into the yeast cells in isolation. Assays for the uptake of fatty acids into the yeast cells can be devised that are similar to those described above and/or those assays that have been illustrated in the Examples. Tests for candidate inhibitors or enhancers of the heterologous FATP can be done in cultures of yeast cells, wherein the yeast cells are incubated with fatty acid substrate and an agent to be tested as an inhibitor or enhancer of FATP function. FATP uptake after a period of time can be measured by analyzing the contents of the yeast cells for fatty acid substrate, as compared with control yeast cells incubated with the fatty acid, but not with the test agent. Yeast cells have the additional advantage, over mammalian cells in culture, for example, that yeast cells can be forced to rely upon fatty acids as their only source of carbon, if the growth medium supplied to the yeast cells is formulated to contain no other source of carbon. Thus, the effect of the heterologous FATP on fatty acid uptake and metabolism in the engineered yeast cells can be amplified. An agent that efficiently blocks transport function of the heterologous FATP could result in death of the yeast cells. Thus, in this case, inhibition of function of the heterologous FATP can result in loss of viability. A simple measure of viability is turbidity of the yeast suspension culture, which can be adapted to a high throughput screening assay for effects of various agents to be tested, using microtiter plates or similar devices for small-volume cultures of the engineered yeast cells.

Cell-free assays can also be used to measure the transport of fatty acids across a membrane, and therefor also to assess a test treatment or test agent for its effect on the rate or extent of fatty acid transport. An isolated FATP, for example in the presence of a detergent that preserves the native 3-dimensional structure of the FATP, or partially purified FATP, can be used in an artificial membrane system typically used to preserve the native conformation and activity of membrane proteins. Such systems include liposomes, artificial bilayers of phospholipids, isolated plasma membrane such as cell membrane fragments, cell membrane fractions, or cell membrane vesicles, and other systems in which the FATP can be properly oriented within the membrane to have transport activity. Assays for transport activity can be performed using methods

analogous to those that can be used in cells engineered to predominantly express one FATP whose function is to be measured. A labeled (e.g., radioactively labeled) fatty acid substrate can be incubated with one side of a bilayer or in a suspension of liposomes constructed to integrate a properly oriented FATP. The accumulation of fatty acids with time can be measured, using appropriate means to detect the label (e.g., scintillation counting of medium on each side of the bilayer, or of the contents of liposomes isolated from the surrounding medium). Assays such as these can be adapted to use for the testing of agents which might interact with the FATP to produce an inhibitory or an enhancing effect on the rate or extent of fatty acid transport. That is, the above-described assay can be done in the presence or absence of the agent to be tested, and the results compared.

For examples of isolation of membrane proteins (ADP/ATP carrier and uncoupling protein), reconstitution into phospholipid vesicles, and assays of transport, see Klingenberg, M. *et al.*, *Methods Enzymol.* 260:369-389 (1995). For an example of a membrane protein (phosphate carrier of *Saccharomyces cerevisiae*) that was purified and solubilized from *E. coli* inclusion bodies, see Schroer, A. *et al.*, *J. Biol. Chem.* 273: 14269-14276 (1998). The Glut1 glucose transporter of rat has been expressed in yeast. A crude membrane fraction of the yeast was prepared and reconstituted with soybean phospholipids into liposomes. Glucose transport activity could be measured in the liposomes (Kasahara, T. and Kasahara, M., *J. Biol. Chem.* 273: 29113-29117 (1998)). Similar methods can be applied to the proteins and polypeptides of the invention.

Another embodiment of the invention is a method for inhibiting fatty acid uptake in a mammal (e.g., a human), comprising administering to the mammal a therapeutically effective amount of an inhibitor of the transport function of one or more of the fatty acid transport proteins, thereby decreasing fatty acid uptake by cells comprising the fatty acid protein(s). Where it is desirable to reduce the uptake of fatty acids, for example, in the treatment of chronic obesity or as a part of a program of weight control or hyperlipidemia control in a human, one or more inhibitors of one or more of the fatty acid transport proteins can be administered in an effective dose, and by

an effective route, for example, orally, or by an indwelling device that can deliver doses to the small intestine. The inhibitor can be one identified by methods described herein, or can be one that is, for instance, structurally related to an inhibitor identified by methods described herein (e.g., having chemical adducts to better stabilize or solubilize the inhibitor). The invention further relates to compositions comprising inhibitors of fatty acid uptake in a mammal, which may further comprise pharmaceutical carriers suitable for administration to a subject mammal, such as sterile solubilizing or emulsifying agents.

A further embodiment of the present invention is a method of enhancing or increasing fatty acid uptake, such as enhancing or increasing LCFA uptake in the small intestine (e.g., to treat or prevent a malabsorption syndrome or other wasting condition) or in the liver (e.g., by an enhancer of FATP5 transport activity to treat acute liver failure) or in the kidney (e.g., by an enhancer of FATP2 transport activity to treat kidney failure). In this embodiment, a therapeutically effective amount of an enhancer of the transport function of one or more of the fatty acid transport proteins can be administered to a mammalian subject, with the result that fatty acid uptake in the small intestine is enhanced. In this embodiment, one or more enhancers of one or more of fatty acid transport proteins is administered in an effective dose and by a route (e.g., orally or by a device, such as an indwelling catheter or other device) which can deliver doses to the gut. The enhancer of FATP function (e.g., an enhancer of FATP4 function) can be identified by methods described herein or can be one that is structurally similar to an enhancer identified by methods described herein.

Aerobic reperfusion of ischemic myocardium is a common clinical event which can occur during such treatments as cardiac surgery, angioplasty, and thrombolytic therapy after a myocardial infarction. During reperfusion, a rapid recovery of myocardial energy production is essential for the complete recovery of contractile function. Not only the extent of recovery of myocardial energy metabolism but also the type of energy substrate used by the heart during reperfusion are important determinants of functional recovery. Circulating fatty acid levels increase following acute

myocardial infarction or during cardiac surgery, such that during and following ischemia the heart muscle can be exposed to very high concentrations of fatty acids (Lopaschuk, G.D. and W. C. Stanley, *Science and Medicine* (November/December 1997)). High plasma fatty acid concentrations increase the severity of ischemic damage

5 in a number of experimental models of cardiac ischemia and have been linked to depression of mechanical function during aerobic reperfusion of previously ischemic hearts. Further data show that modifying fatty acid utilization can be beneficial for heart function in ischemia and can be a useful approach for the treatment of angina. See, e.g., Desideri and Celegon, *Am. J. Cardiol.* 82(5A):50K-53K; Lopaschuk, *Am. J.*

10 *Cardiol.* 82(5A):14K-17K. Plasma fatty acid concentrations can be reduced by administering to a human subject or other mammal an effective amount of an inhibitor of a FATP such as FATP2 or FATP4, thereby providing a way of reducing fatty acid utilization by the heart.

In a further embodiment of the invention, a therapeutically effective amount of

15 an inhibitor of hsFATP6 can be administered to a human patient by a suitable route, to reduce the uptake of fatty acids by cardiac muscle. This treatment is desirable in patients who are diagnosed as having, or who are at risk of, abnormal accumulations of fatty acids in the heart or a detrimentally high rate of uptake of fatty acids into the heart, because of ischemic heart disease, or following ischemia or trauma to the heart.

20 The invention further relates to antibodies that bind to an isolated or recombinant fatty acid transport protein of the FATP family, including portions of antibodies, which can specifically recognize and bind to one or more FATPs. The antibodies and portions thereof of the invention include those which bind to one or more FATPs of mouse or other mammalian species. In a preferred embodiment, the

25 antibodies specifically bind to a naturally occurring FATP of humans. The antibodies can be used in methods to detect or to purify a protein of the present invention or a portion thereof by various methods of immunoaffinity chromatography, to inhibit the function of a protein in a method of therapy, or to selectively inactivate an active site, or to study other aspects of the structure of these proteins, for example.

The antibodies of the present invention can be polyclonal or monoclonal. The term antibody is intended to encompass both polyclonal and monoclonal antibodies. Antibodies of the present invention can be raised against an appropriate immunogen, including proteins or polypeptides of the present invention, such as an isolated or
5 recombinant FATP1, FATP2, FATP3, FATP4, FATP5, FATP6, mtFATP, ceFATPa, ceFATPb, scFATP or portions thereof, or synthetic molecules, such as synthetic peptides (e.g., conjugated to a suitable carrier). Preferred embodiments are antibodies that bind to any of the following: hsFATP1, hsFATP2, hsFATP3, hsFATP4, hsFATP5 or hsFATP6. The immunogen can be a polypeptide comprising a portion of a FATP
10 and having at least one function of a fatty acid transport protein, as described herein.

The term antibody is also intended to encompass single chain antibodies, chimeric, humanized or primatized (CDR-grafted) antibodies and the like, as well as chimeric or CDR-grafted single chain antibodies, comprising portions from more than one species. For example, the chimeric antibodies can comprise portions of proteins
15 derived from two different species, joined together chemically by conventional techniques or prepared as a single contiguous protein using genetic engineering techniques (e.g., DNA encoding the protein portions of the chimeric antibody can be expressed to produce a contiguous protein chain. See, e.g., Cabilly et al., U.S. Patent No. 4,816,567; Cabilly *et al.*, European Patent No. 0,125,023 B1; Boss *et al.*, U.S.
20 Patent No. 4,816,397; Boss *et al.*, European Patent No. 0,120,694 B1; Neuberger, M.S. *et al.*, WO 86/01533; Neuberger, M.S. *et al.*, European Patent No. 0,194,276 B1; Winter, U.S. Patent No. 5,225,539; Winter, European Patent No. 0,239,400 B1; Queen *et al.*, U.S. Patent No. 5,585,089; and Queen *et al.*, European Patent No. EP 0 451 216 B1. See also, Newman, R. *et al.*, *BioTechnology*, 10:1455-1460 (1992), regarding
25 primatized antibody, and Ladner *et al.*, U.S. Patent No. 4,946,778 and Bird, R.E. *et al.*, *Science*, 242:423-426 (1988) regarding single chain antibodies.)

Whole antibodies and biologically functional fragments thereof are also encompassed by the term antibody. Biologically functional antibody fragments which can be used include those fragments sufficient for binding of the antibody fragment to a

FATP to occur, such as Fv, Fab, Fab' and F(ab')₂ fragments. Such fragments can be produced by enzymatic cleavage or by recombinant techniques. For instance, papain or pepsin cleavage can generate Fab or F(ab')₂ fragments, respectively. Antibodies can also be produced in a variety of truncated forms using antibody genes in which one or more stop codons have been introduced upstream of the natural stop site. For example, a chimeric gene encoding a F(ab')₂ heavy chain portion can be designed to include DNA sequences encoding the CH₁ domain and hinge region of the heavy chain.

Preparation of immunizing antigen (whole cells comprising FATP on the cell surface or purified FATP), and polyclonal and monoclonal antibody production can be performed using any suitable technique. A variety of methods have been described (See e.g., Kohler *et al.*, *Nature*, 256: 495-497 (1975) and *Eur. J. Immunol.* 6: 511-519 (1976); Milstein *et al.*, *Nature* 266: 550-552 (1977); Koprowski *et al.*, U.S. Patent No. 4,172,124; Harlow, E. and D. Lane, 1988, *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory: Cold Spring Harbor, NY); Chapter 11 In *Current Protocols In Molecular Biology*, Vol. 2 (containing supplements up through Supplement 42, 1998), Ausubel, F.M. *et al.*, eds., (John Wiley & Sons: New York, NY)). Generally, a hybridoma can be produced by fusing a suitable immortal cell line (e.g., a myeloma cell line such as SP2/0) with antibody producing cells. The antibody producing cells, preferably those obtained from the spleen or lymph nodes, can be obtained from animals immunized with the antigen of interest. Immunization of animals can be by introduction of whole cells comprising fatty acid transport protein on the cell surface. The fused cells (hybridomas) can be isolated using selective culture conditions, and cloned by limiting dilution. Cells which produce antibodies with the desired specificity can be selected by a suitable assay (e.g., ELISA).

Other suitable methods of producing or isolating antibodies (including human antibodies) of the requisite specificity can be used, including, for example, methods which select recombinant antibody from a library (e.g., Hoogenboom *et al.*, WO 93/06213; Hoogenboom *et al.*, U.S. Patent No. 5,565,332; WO 94/13804, published June 23, 1994; and Dower, W.J. *et al.*, U.S. Patent No. 5,427,908), or which rely upon

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immunization of transgenic animals (e.g., mice) capable of producing a full repertoire of human antibodies (see e.g., Jakobovits *et al.*, *Proc. Natl. Acad. Sci. USA*, 90: 2551-2555 (1993); Jakobovits *et al.*, *Nature*, 362:255-258 (1993); Lonberg *et al.*, U.S. Patent No. 5,569,825; Lonberg *et al.*, U.S. Patent No. 5,545,806; Surani *et al.*, U.S. Patent No. 5,545,807; and Kucherlapati, R. *et al.*, European Patent No. EP 0 463 151 B1).

Another aspect of the invention is a method for directing an agent to cardiac muscle. The differential expression of FATP6 in cardiac muscle but not in other tissue types allows for the specific targeting of drugs, diagnostic agents, tagging labels, histological stains or other substances specifically to cardiac muscle. A targeting vehicle can be used for the delivery of such a substance. Targeting vehicles which bind specifically to FATP6 can be linked to a substance to be delivered to the cells of cardiac muscle. The linkage can be, for instance, via one or more covalent bonds, or by high affinity non-covalent bonds. A targeting vehicle can be an antibody, for instance, or other compound (e.g., a fatty acid or fatty acid analog) which binds to FATP6 with high specificity.

Targeting vehicles specific to the heart-specific protein FATP6 have *in vivo* (e.g., therapeutic and diagnostic) applications. For example, an antibody which specifically binds to FATP6 can be conjugated to a drug to be targeted to the heart (e.g., a cardiac glycoside to treat congestive heart failure, or β -adrenergic agents, sodium channel blockers or calcium channel blockers to treat arrhythmias). A substance (e.g., a radioactive substance) which can be detected (e.g., a label) *in vivo* can also be linked to a targeting vehicle which specifically binds to a heart-specific protein such as FATP6, and the conjugate can be used as a labeling agent to identify cardiac muscle cells.

Targeting vehicles specific to FATP6 find further applications *in vitro*. For example, an FATP6-specific targeting vehicle, such as an antibody (a polyclonal preparation or monoclonal) which specifically binds to FATP6, can be linked to a substance which can be used as a stain for a tissue sample (e.g., horseradish peroxidase) to provide a method for the identification of cardiac muscle in a sample, as can be used in embryology studies, for example.

In a similar manner, an agent can be directed to the liver of a mammal, as FATP5 is expressed in liver but not in other tissue types. A targeting vehicle which specifically binds to FATP5 can be conjugated to a drug for delivery of the drug to the liver, such as a drug to treat hepatitis, Wilson's disease, lipid storage diseases and liver cancer. As with targeting vehicles specific to FATP6, targeting vehicles specific to FATP5 can be used in studying tissue samples *in vitro*.

The invention also relates to compositions comprising a modulator of FATP function. The term "modulate" as used herein refers to the ability of a molecule to alter the function of another molecule. Thus, modulate could mean, for example, inhibit, antagonize, agonize, upregulate, downregulate, induce, or suppress. A modulator has the capability of altering function of its target. Such alteration can be accomplished at any stage of the transcription, translation, expression or function of the protein, so that, for example, modulation of a target gene can be accomplished by modulation of the DNA or RNA encoding the protein, and the protein itself.

Antagonists or agonists (inhibitors or enhancers) of the FATPs of the invention, antibodies that bind a FATP, or mimetics of a FATP can be employed in combination with a non-sterile or sterile carrier or carriers for use with cells, tissues or organisms, such as a pharmaceutical carrier suitable for administration to a mammalian subject. Such compositions comprise, for instance, a media additive or a therapeutically effective amount of an inhibitor or enhancer compound to be identified by an assay of the invention and a pharmaceutically acceptable carrier or excipient. Such carriers may include, but are not limited to, saline, buffered saline, dextrose, water, ethanol, surfactants, such as glycerol, excipients such as lactose and combinations thereof. The formulation can be chosen by one of ordinary skill in the art to suit the mode of administration. The chosen route of administration will be influenced by the predominant tissue or organ location of the FATP whose function is to be inhibited or enhanced. For example, for affecting the function of FATP4, a preferred administration can be oral or through a tube inserted into the stomach (e.g., direct stomach tube or nasopharyngeal tube), or through other means to accomplish delivery to the small

intestine. The invention further relates to diagnostic and pharmaceutical packs and kits comprising one or more containers filled with one or more of the ingredients of the aforementioned compositions of the invention.

Compounds of the invention which are FATPs, FATP fusion proteins, FATP
5 mimetics, FATP gene-specific antisense poly- or oligonucleotides, inhibitors or
enhancers of a FATP may be employed alone or in conjunction with other compounds,
such as therapeutic compounds. The pharmaceutical compositions may be administered
in any effective, convenient manner, including administration by topical, oral, anal,
vaginal, intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal,
10 transdermal or intradermal routes, among others. In therapy or as a prophylactic, the
active agent may be administered to an individual as an injectable composition, for
example as a sterile aqueous dispersion, preferably isotonic.

Alternatively, the composition may be formulated for topical application, for
example, in the form of ointments, creams, lotions, eye ointments, eye drops, ear drops,
15 mouthwash, impregnated dressings and sutures and aerosols, and may contain
appropriate conventional additives, including, for example, preservatives, solvents to
assist drug penetration, and emollients in ointments and creams. Such topical
formulations may also contain compatible conventional carriers, for example cream or
ointment bases, and ethanol or oleyl alcohol for lotions.

20 In addition, the amount of the compound will vary depending on the size, age,
body weight, general health, sex, and diet of the host, and the time of administration, the
biological half-life of the compound, and the particular characteristics and symptoms of
the disorder to be treated. Adjustment and manipulation of established dose ranges are
well within the ability of those of skill in the art.

25 A further aspect of the invention is a method to identify a polymorphism, or the
presence of an alternative or variant allele of a gene in the genome of an organism (of
interest here, genes encoding FATPs). As used herein, polymorphism refers to the
occurrence of two or more genetically determined alternative sequences or alleles in a
population. A polymorphic locus may be as small as a base pair. Polymorphic markers

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include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The first identified allelic form, or the most frequently occurring form can be
5 arbitrarily designated as the reference (usually, "wildtype") form, and other allelic forms are designated as alternative (sometimes, "mutant" or "variant"). Diploid organisms may be homozygous or heterozygous for allelic forms.

An "allele" or "allelic sequence" is an alternative form of a gene which may result from at least one mutation in the nucleotide sequence. Alleles may result in
10 altered mRNAs or polypeptides whose structure or function may or may not be altered. Any given gene may have none, one, or many allelic forms (polymorphism). Common mutational changes which give rise to alleles are generally ascribed to natural deletions, additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

15 Several different types of polymorphisms have been reported. A restriction fragment length polymorphism (RFLP) is a variation in DNA sequence that alters the length of a restriction fragment (Botstein *et al.*, *Am. J. Hum. Genet.* 32:314-331 (1980)). The restriction fragment length polymorphism may create or delete a restriction site, thus changing the length of the restriction fragment. RFLPs have been widely used in
20 human and animal genetic analyses (see WO 90/13668; WO 90/11369; Donis-Keller, *Cell* 51:319-337 (1987); Lander *et al.*, *Genetics* 121:85-99 (1989)). When a heritable trait can be linked to a particular RFLP, the presence of the RFLP in an individual can be used to predict the likelihood that the individual will also exhibit the trait.

Other polymorphisms take the form of short tandem repeats (STRs) that include
25 tandem di-, tri- and tetra-nucleotide repeated motifs. These tandem repeats are also referred to as variable number tandem repeat (VNTR) polymorphisms. VNTRs have been used in identity and paternity analysis (US 5,075,217; Armour *et al.*, *FEBS Lett.* 307:113-115 (1992); Horn *et al.*, WO 91/14003; Jeffreys, EP 370,719), and in a large number of genetic mapping studies.

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compared to the reference as having a variant allele, using the same or comparable amplification procedures, and determining whether the reference DNA and test DNA differ in DNA sequence in the FATP gene, whether in a coding or a noncoding region, wherein, if the test DNA differs in sequence from the reference DNA, the test DNA
5 comprises a variant allele of a human FATP gene. The following is a discussion of some of the methods by which it can be determined whether the reference FATP DNA and test FATP DNA differ in sequence.

Direct Sequencing. The direct analysis of the sequence of variant alleles of the present invention can be accomplished using either the dideoxy chain termination
10 method or the Maxam and Gilbert method (see Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Press, New York 1989; Zyskind *et al.*, *Recombinant DNA Laboratory Manual*, Acad. Press, 1988)).

Denaturing Gradient Gel Electrophoresis. Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient
15 gel electrophoresis. Different alleles can be identified based on the different sequence-dependent strand dissociation properties and electrophoretic migration of DNA in solution (chapter 7 in Erlich, ed. *PCR Technology, Principles and Applications for DNA Amplification*, W.H. Freeman and Co., New York, 1992).

Single-strand Conformation Polymorphism Analysis. Alleles of target
20 sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita *et al.*, *Proc. Natl. Acad. Sci. USA* 86:2766-2770 (1989). Amplified PCR products can be generated as described above, and heated or otherwise denatured, to form single-stranded amplification products.
25 Single-stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence differences between alleles of target sequences.

Detection of Binding by Protein That Binds to Mismatches. Amplified DNA comprising the FATP gene or portion of the gene of interest from genomic DNA, for example, of a normal individual is prepared, using primers designed on the basis of the DNA sequences provided herein. Amplified DNA is also prepared, in a similar manner,
5 from genomic DNA of an individual to be tested for bearing a distinguishable allele. The primers used in PCR carry different labels, for example, primer 1 with biotin, and primer 2 with ³²P. Unused primers are separated from the PCR products, and the products are quantitated. The heteroduplexes are used in a mismatch detection assay using immobilized mismatch binding protein (MutS) bound to nitrocellulose. The
10 presence of biotin-labeled DNA wherein mismatched regions are bound to the nitrocellulose via MutS protein, is detected by visualizing the binding of streptavidin to biotin. See WO 95/12689. MutS protein has also been used in the detection of point mutations in a gel-mobility-shift assay (Lishanski, A. *et al.*, *Proc. Natl. Acad. Sci. USA* 91:2674-2678 (1994)).

15 Other methods, such as those described below, can be used to distinguish a FATP allele from a reference allele, once a particular allele has been characterized as to DNA sequence.

Allele-specific probes. The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki *et al.*, *Nature* 324:163-166 (1986);
20 Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed so that they hybridize to a segment of a target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in the respective segments from the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant
25 difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position (e.g., in a 15-mer at the 7 position; in a 16-mer, at either the 8 or

9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

Allele-specific Primers. An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism, and only primes amplification of an allelic form to which the primer exhibits perfect complementarity. See Gibbs, *Nucleic Acid Res.* 17:2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers, resulting in a detectable product which indicates the particular allelic form is present. A control is usually performed with a second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarity to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer (see, e.g., WO 93/22456).

Gene Chips. Allelic variants can also be identified by hybridization to nucleic acids immobilized on solid supports (gene chips), as described, for example, in WO 95/11995 and U.S. Patent No. 5,143,854, both of which are incorporated herein by reference. WO 95/11995 describes subarrays that are optimized for detection of a characterized variant allele. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence.

The present method is illustrated by the following examples, which are not intended to be limiting in any way.

EXAMPLES

Materials and Methods

5 The following Materials and Methods were used in the work described in Examples 1-5.

Sequence Alignment of FATP Clones. The DNA sequence for mouse FATP1 was obtained from the National Center for Biotechnology Information nonredundant database. cDNAs for mmFATP2, 3, 4, and 5 were obtained by screening mouse
10 expression libraries (purchased from GIBCO/BRL) with probes derived from the cloned expressed sequence tags (ESTs) (Research Genetics, Huntsville, AL). Full-length clones were obtained for mmFATP2 and 5 and partial sequences for mmFATP3 and 4. The sequences described herein have been deposited in the GenBank database (Accession Nos. FATP2, AF072760; FATP3, AF072759; FATP4, AF072758; FATP5,
15 AF072757).

Neither FATP2 nor FATP5 contains an in-frame stop codon upstream of the putative initiator methionine; initiator methionines were assigned by homology with that in mmFATP1 and by the presence of a signal sequence immediately after it. The *Mycobacterium tuberculosis*, *Caenorhabditis elegans*, and *Saccharomyces cerevisiae*
20 sequences were present in the dbEST database as part of the sequencing projects for these organisms. Sequences were aligned utilizing a ClustalX algorithm and the resulting alignment exported to SeqVu. Homologous amino acid substitutions are boxed in Figure 1 and were determined using the Dayhoff 250 method with a 50% homology cutoff.

25 Cell Transfection and LCFA Uptake. COS cells were cotransfected using the DEAE-dextran method with the mammalian expression vector pCDNA 3.1 (Invitrogen) expressing the gene for CD2 (pCDNA-CD2) in combination with either a pCDNA 3.1 or pCMVSPORT2 (GIBCO/BRL) expression vector containing one of the murine or

nematode *FATP* genes (*pCDNA-mmFATP1*, *pCDNA-FATP2*, *pCMVSPORT-FATP5*, *pCDNA-ceFATPb*). Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2(PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analogue

5 (Molecular Probes). Briefly, cells were washed twice with PBS (phosphate buffered saline) and stained with PE-CD2 at 4°C for 30 min in PBS containing 10% fetal calf serum. They were then washed three times with PBS/fetal calf serum for 5 min followed by an incubation for 2 min at 37°C in fatty acid uptake solution, which contained 0.1 μ M BODIPY-FA and 0.1% fatty acid-free BSA (bovine serum albumin)
 10 in PBS (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). After 2 min, the cells were washed four times with ice-cold PBS/0.1% BSA. The cells were then removed from the plates with PBS containing 5 mM EDTA and resuspended in PBS containing 10% fetal calf serum and 10 mM EDTA. PE-CD2 and BODIPY-FA fluorescence were measured using a FACScan (Becton Dickinson). COS cells were gated on forward
 15 scatter (FSC) and side scatter (SS). Cells exhibiting more than 300 CD2 fluorescence units (dsim) representing 15% of all cells were deemed CD2 positive and their BODIPY-FA fluorescence was quantitated.

E. coli-Based LCFA Uptake Assay. The full-length coding region of mtFATP and a control protein, the mammalian transcription factor TFE3, were subcloned into the
 20 inducible, prokaryotic expression vector pET (Novagen). Expression was induced with 1 mM isopropyl β -D-thiogalactoside (IPTG) for 1 hour, or cells were left uninduced. Cells were washed in PBS/0.1% BSA and resuspended in 1 ml PBS/0.1% BSA containing 0.1 μ M [3 H]palmitate (NEN) at 37°C. Uptake was stopped after the indicated incubation time by transferring the cells onto filter paper using a cell harvester
 25 (Brandel, Bethesda, MD). Filters were washed extensively with ice-cold PBS/0.1% BSA, and [3 H]palmitate was quantitated by scintillation counting.

Northern Blots. Northern blot analysis of murine FATP expression was done using poly(A) mRNA blots (Clontech). Probes of each of the FATPs were derived from the 3' untranslated regions of each gene and were <60% identical in sequence. Probes

were labeled by random priming (Boehringer Mannheim) and hybridized at 65°C. Blots were extensively washed in 0.2% SSC/0.1% SDS at 65°C.

Generation of Phylogenetic Trees. Complete and partial sequences for *FATP* genes from human, rat, mouse, puffer fish, *Drosophila melanogaster*, *C. elegans*, *S. cerevisiae*, and *M. tuberculosis* were aligned using ClustalX. A homologous region of 48 amino acids (residues 472-519 in mmFATP1) from all of the genes was used to determine phylogenetic relationship within ClustalX. Based on these data a phylogenetic tree was generated using Tree View PPC (Figure 5).

Nomenclature. It is proposed that the *FATP* genes be given a species specific prefix (mm, *Mus musculus*; hs, *Homo sapiens*; mt, *M. tuberculosis*; dm, *D. melanogaster*; ce, *C. elegans*, sc, *S. cerevisiae*) and numbered such that mammalian homologues in different species share the same number but differ in their prefix. Since the two *C. elegans* genes cannot be paired with a specific human or mouse *FATP*, they have been designated *ceFATPa* and *ceFATPb*.

Example 1: Identification of Novel Mammalian FATPs

The National Center for Biotechnology Information EST database was screened, using the mouse *FATP* protein sequence (mmFATP1), to identify novel *FATPs*. This strategy led to the identification of more than 50 murine EST sequences which could be assembled into five distinct contiguous DNA sequences (contigs). One contig was identical to the previously cloned *FATP*, which has been renamed *FATP1*. Another, which has been renamed *FATP2*, is the murine homologue of a rat gene previously identified by others as a very long chain acyl-CoA synthase (Uchiyama, A., Aoyama, T., Kamijo, K., Uchida, Y., Kondo, N., Orii, T. & Hashimoto, T. (1996) *J. Biol. Chem.* 271:30360-30365). The other three contigs represented novel genes (*FATP3*, 4, and 5). Full-length clones for *FATP2* and *FATP5* and nearly complete sequences for *FATP3* and 4 (Figure 1) were obtained by screening cDNA libraries made from mouse day 10.5 embryos and adult liver. Also identified were human homologues for each of the murine genes in the EST database. A sixth human gene was also identified; whether

this gene is also present in the mouse will require additional studies. Map positions are given in Tables 2 and 3.

The genetic loci for all of the human genes, with the exception of FATP5 which was already mapped as an unknown EST, were determined using the radiation hybrid
5 panels. The map positions given below show the distance (in centiRays) from the closest framework marker. As a guideline, there are approximately 300kb/cR.

Table 2. Mapping Data for Human Genes

	hsFATP1	Chromosome Chr19 places 13.35 cR from WI-6344 (lod>3.0)
10	hsFATP2	Chromosome Chr15 places 4.92 cR from D15S126 (lod>3.0)
	hsFATP3	Chromosome Chr1 places 13.24 cR from WI-2862 (lod>3.0)
15	hsFATP4	Chromosome Chr9 places 7.80 cR from WI-9685 (lod>3.0)
	hsFATP5	unknown EST previously mapped to near D19S418
	hsFATP6	Chromosome Chr5 places 1.41 cR from WI-4907 (lod>3.0)

The mouse map is an internal backcross panel consisting of 188 mouse
20 backcross DNA's plus 4 controls (B6, Spretus, F1, Water). The backcross was constructed by crossing B6 by Spretus animals and then crossing those F1's back to B6. Mapping is accomplished by taking advantage of recombinational events during meiosis, and the use of PCR primers to detect the differences (by size or re-annealing events) at any given locus between the B6 and Spretus allele.

25 For the purposes of mapping, a novel set of primers (gene of interest) is used to amplify from all 188 DNA's and then typed as being a B6 ("B") or a Spretus ("S"). This

string of B's and S's is entered into the Map Manager program, which does a best fit calculation by comparing the string of 188 typings from the gene of interest to all loci already extant in the panel, for all 20 chromosomes. The gene of interest is then assigned to a particular area on a particular chromosome according to a number of parameters, including the minimalization of double cross-overs, and the highest LOD scores. Indicated in Table 3 are distances to the closest markers on either side of the FATP locus.

Table 3. Mapping Data for Mouse Genes

10	mmFATP1	Chromosome 8 places 2.82 cM from D8Mit132 (lod 43.4) and 1.81 cM from D8Mit74 (lod 43.5)
	mmFATP2	Chromosome 2 places 1.29 cM from D2Mit258 (lod 47.9) and 1.75 cM from D2NDS3 (lod 44.9)
15	mmFATP3	Chromosome 3 places 2.54 cM from D3Mit22 (lod 29.5) and 19.62 cM from D3Mit42 (lod 13.6)
20	mmFATP4	Chromosome 2 places 13.78 cM from D2Mit1 (lod 22.9) and 3.85 cM from D2Mit65 (lod 41.9)
	mmFATP5	Chromosome 7 places 7.28 cM proximal of D7Mit21 (lod 28.3)

Example 2: Assessment of Function

The ability of the newly identified mouse genes to function as fatty acid transporters was assessed using a fluorescence-activated cell sorting-based assay. COS cells were transiently cotransfected with expression vectors encoding the cell surface

protein CD2 and either mmFATP1, mmFATP2, or mmFATP5, respectively. Two days after transfection, COS cells were stained with an antibody to CD2 and then incubated with a BODIPY-labeled fatty acid [BODIPY-FA, (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436)]. The cells were then washed extensively, lifted off the dish, and

5 analyzed by fluorescence-activated cell sorting. As judged by the number of CD2-positive cells, the transfection efficiency was approximately 20-30%. Fatty acid uptake was quantitated in the transiently transfected COS cells by measuring the BODIPY-FA fluorescence of the CD2-positive cells. Expression of CD2 had no effect on fatty acid uptake as shown by the finding that COS cells expressing only the transfected CD2

10 cDNA (CD2-positive) had the same low level of BODIPY-FA uptake as did untransfected (CD2-negative) control cells (Figure 2A, control). In COS cells cotransfected with CD2 and mmFATP1, mmFATP2, or mmFATP5, uptake of BODIPY-FA by the transfected (CD2-positive) cells was increased between 15- to 90-fold over control (CD2 cDNA only) cells (Figures 2A-2D).

15 Example 3: Expression Patterns of Murine FATPs

Expression patterns of members of the murine *FATP* gene family were characterized by Northern blot analysis; to avoid cross-hybridization, the probes used were from the 3' untranslated region of these genes, which are less than 60% identical in sequence. The expression pattern of FATP1 agrees with that previously found

20 (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). Here, expression was seen primarily in heart and kidney. FATP2 is expressed almost exclusively in liver and kidney, which corresponds to the reported tissue distribution of the rat homologue [very long chain acyl-CoA (VLACS)] as assessed by Western blotting (Uchiyama, A., Aoyama, T., Kamijo, K., Uchida, Y., Kondo, N., Orii, T. & Hashimoto, T. (1996) *J. Biol. Chem.* 271:30360-30365). FATP3 is present in lung, liver, and testis. FATP5 is

25 expressed only in liver and cannot be detected in other tissues even when the blot is overexposed. The human homologue of FATP5 is also liver specific and is not expressed in a wide array of other tissues tested, including fetal liver.

Example 4: FATPs Are Evolutionarily Conserved

The EST database was searched, using sequences conserved among the five murine FATP genes, for *FATP* genes in other organisms. Two homologues were found in *C. elegans* and one in *M. tuberculosis*. One of the *C. elegans* genes was cloned from a cDNA library and expressed in COS cells, as described for the murine FATPs.

Overexpression of the nematode FATP resulted in a 15-fold increase of BODIPY-FA uptake compared with control cells (Figure 3). The mycobacterial *FATP* gene was isolated from a phage library and assessed for its ability to facilitate fatty acid uptake. *E. coli* transformed with a prokaryotic, isopropyl β -D-thiogalactoside-inducible expression vector containing the mycobacterial *FATP* gene demonstrated a significant increase in the rate of [3 H]palmitate uptake after induction, compared with uninduced bacteria or *E. coli* transformed with a control protein (Figure 4). Novel *FATP* genes were also identified in *F. rubripes* (puffer fish) and *D. melanogaster*.

Example 5: Phylogenetic Tree of FATPs

Faergeman *et al.* (Faergeman, N.J., DiRusso, C.C., Elberger, A., Knudsen, J. & Black, P. N. (1997) *J. Biol. Chem.* 272:8531-8538) identified three regions of very strong conservation between the *scFATP* and *mmFATP1* genes. The sequences of the FATPs were compared over a 311-amino acid FATP "signature sequence" which includes these conserved regions corresponding to amino acids 246-557 in *mmFATP1* (underlined in Figure 1). When compared with the National Center for Biotechnology Information nonredundant database, only one region of the "FATP signature sequence" shows significant homology to other proteins. This small stretch of amino acids (underlined in Fig. 1) is an AMP-binding motif found in a multitude of other proteins, such as acyl-CoA synthase, several CoA lipases, and gramicidin S synthetase component II (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). The relevance of this motif to fatty acid transport is unclear. Other highly conserved regions among the FATPs, including long stretches of amino acids >90% identical from mycobacteria to humans, are not found in any other class of proteins. A 48-amino acid segment of the

FATP signature sequence was used to construct a phylogenetic tree (Figure 5). Each of the human and mouse genes form their own branch; hsFATP6, which as yet has no murine homologue, is most closely related to hsFATP3 and mmFATP3. As expected, mVLACS is closer in sequence to mmFATP2 than to hsFATP2. The *FATP* genes of invertebrates i.e., *C. elegans* and *D. melanogaster*, are most closely related to each other. Surprisingly, the mycobacterial gene is more closely related to the human and mouse *FATP5* genes than to the FATPs of any of the lower organisms. Whether this reflects coevolution of the mycobacterial and human genes awaits further study.

Materials and Methods

The following materials and methods were used in the work described in Examples 6-10.

Isolation of full-length human FATP1 and 4

Full-length clones encoding human FATP1 and human FATP4 were identified by searching databases for sequences similar to murine FATP1-5 coding regions using the BlastX algorithm (Altschul *et al.*, *J. Mol. Biol.* 215: 403-410, 1990).

A concatamer of nucleotide sequences comprising the coding sequences of mmFATP1 (Genbank Accession U15976), mmFATP2, mmFATP3 (SEQ ID NO:6), mmFATP4 (SEQ ID NO:8) and mmFATP5 (SEQ ID NO:10) was used to search the Millennium database using the BLASTX algorithm. Sequences with a score >150 were evaluated for whether they represented known FATP coding sequences.

Human clones with similarity to the 5' end of murine FATP sequences were sequenced completely. Clones encoding full-length human FATP1 were obtained from a heart cDNA library constructed in the mammalian expression vector pMET7 (Tartaglia *et al.*, *Cell*, 83: 1263-1271, 1995). Clones encoding full-length human FATP4 were obtained from a spleen cDNA library constructed in the mammalian expression vector pMET7.

Isolation of full-length human FATP6

Several clones encoding human FATP6 were identified by searching public databases as described above. Five clones were analyzed further by restriction digestion and DNA sequencing. One of these clones (Genbank Accession # AA412064) appeared
5 to be full-length and its entire insert was sequenced.

DNA Sequence Analysis

Sequences were aligned with the DNASTar program using the Clustal method. Hydrophobicity plots were generated with DNA Strider using the Kyte Doolittle method.

10 In situ hybridization

Tissues were collected from 8 week old C57/B16 mice. Tissues were fresh frozen, cut on a cryostat at 10 μ m thickness and mounted on Superfrost Plus slides (VWR). Sections were air dried for 20 minutes and then incubated with ice cold 4% paraformaldehyde (PFA)/phosphate buffered saline (PBS) for 10 minutes. Slides were
15 washed 2 times 5 minutes with PBS, incubated with 0.25% acetic anhydride/1 M triethanolamine for 10 minutes, washed with PBS for 5 minutes and dehydrated with 70%, 80%, 95% and 100% ethanol for 1 minute each. Sections were incubated with chloroform for 5 minutes. Hybridizations were performed with 35 S-radiolabeled (5×10^7 cpm/ml) cRNA probes generated from the 3' untranslated regions of mouse FATPs by
20 PCR followed by *in vitro* transcription in the presence of 50% formamide, 10% dextran sulfate, 1x Denhardt's solution, 600 mM NaCl, 10 mM DTT, 0.25% SDS and 10 μ g/ml tRNA for 18 hours at 55°C. After hybridization, slides were washed with 10 mM Tris-HCl pH 7.6, 500 mM NaCl, 1 mM EDTA (TNE) for 10 minutes, incubated in 40 μ g/ml RNase A in TNE at 37°C for 30 minutes, washed in TNE for 10 minutes,
25 incubated once in 2x SSC at 60°C for 1 hour, once in 0.2x SSC at 60°C for 1 hour, once in 0.2x SSC at 65°C for 1 hour and dehydrated with 50%, 70%, 80%, 90% and 100% ethanol. Localization of mRNA transcripts was detected by dipping slides in Kodak

NBT-2 photoemulsion and exposing for 7 days at 4°C, followed by development with Kodak Dektol developer. Slides were counter stained with haematoxylin and eosin and photographed. Controls for the in situ hybridization experiments include the use of a sense probe which showed no signal above background in all cases.

5 Northern Blotting

Human mRNA blots were obtained from Invitrogen or Clontech. PCR fragments from the 3' untranslated regions of human FATPs were used as probes. Blots were probed with ³²P-labeled DNA probes using the Rapid-Hyb buffer (Amersham) according to the manufacturer's instructions.

- 10 Cell transfection and LCFA uptake. COS cells were cotransfected, using lipofectamine (GIBCO BRL) according to the manufacturer's instructions, with the mammalian expression vector pCDNA3.1 (Invitrogen) expressing the gene for CD2 in combination with a pMET7 expression vector (Tartaglia *et al.*, *Cell*, 83:1263-1271, 1995) containing hsFATP1 (pMET7-hsFATP1) or hsFATP4 (pMET7-hsFATP4) or
15 pMET7 alone. Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2 (PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analog (Molecular Probes) as described above.

Example 6: Determination of Expression of mmFATPs

- 20 mmFATP4, and to lesser extent mmFATP2, are expressed at high levels in the brush border layer of the small intestine.

- Cell transfection and LCFA uptake. COS cells were cotransfected, using lipofectamine (GIBCO BRL) according to the manufacturer's instructions, with the mammalian expression vector pCDNA3.1 (Invitrogen) expressing the gene for CD2 in
25 combination with a pMET7 expression vector (Tartaglia *et al.*, *Cell*, 83:1263-1271, 1995) containing hsFATP1 (pMET7-hsFATP1) or hsFATP4 (pMET7-hsFATP4) or pMET7 alone. Two days after transfection, cells were assayed for CD2 expression with

a phycoerythrin-coupled anti-CD2 (PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analog (Molecular Probes) as described above.

Absorption of dietary fat requires transport of free fatty acids across the apical
5 membrane of epithelial cells in the small intestine. Previous studies suggested that this transport is protein-mediated; however, the transport protein had not yet been identified. In situ hybridization was performed on each of the three regions of the small intestine -- duodenum, jejunum and ileum -- as well as the colon, using probes from the 3' untranslated regions of mmFATP1, mmFATP2, mmFATP3, mmFATP4 and
10 mmFATP5, to determine whether any of the mouse FATPs are expressed in the small intestine. It was expected that a protein involved in fatty acid absorption would be expressed in the epithelial cells of the small intestine, but absent from the colon.

Expression of mmFATPs in the jejunum was identical to that in the ileum in all cases. High levels of mmFATP4 mRNA were present in the epithelial cells of the
15 jejunum and ileum, and lower, but significant, amounts were detected in the epithelial cells of the duodenum. Significantly, FATP4 mRNA was absent from other cell types of the small intestine and no FATP4 mRNA could be detected in any of the cells of the colon. FATP2 mRNA was present in the epithelial cells of the duodenum at a level similar to that of FATP4, but was present at lower levels in the jejunum and ileum. No
20 signals above background were detected for mmFATP1, mmFATP3 and mmFATP5 in any of the intestinal tissues. mmFATP3 and FATP5 were clearly detectable by in situ hybridization in adult liver and mmFATP1 could be detected in a variety of tissues on a whole embryo in situ, indicating that the FATP1, 3, and 5 probes were working.

mmFATP4 expression is predominant in the small intestine compared to the
25 other organs of the mouse embryo. In the small intestine, FATP4 expression is limited to differentiated enterocytes, while no signal is detected in the connective tissue or the undifferentiated epithelial cells in the crypts. Differentiated enterocytes are known to be the cells that mediate the uptake of fatty acids. FATP4 is specifically and strongly expressed in the epithelial cells of adult murine duodenum and ileum but not colon.

Other FATPs, such as FATP5, are not expressed in the small intestine. Thus, FATP4 is the major FATP in the mouse small intestine. Given its high level of expression, it is likely that FATP4, and to a lesser extent FATP2, play an important role in the absorption of fatty acids.

5 mmFATP2, and mmFATP5 are expressed in hepatocytes

Northern analysis of mmFATP2, mmFATP3, mmFATP4 and mmFATP5 showed expression in the liver. To determine whether these proteins are present in hepatocytes or other cells types present in liver homogenates, in situ hybridizations were performed. mmFATP2, and mmFATP5 mRNA was clearly present in
10 hepatocytes, and was not concentrated in other cell types such as endothelial cells or macrophages. No signal above background was detected for mmFATP1 in any of the cell types in the liver, consistent with the results of the Northern blotting.

Example 7: Isolation and Sequence Analysis of Full-length Human FATP1 and Full-length Human FATP4

15 To identify human cDNA clones encoding FATP family members, Millennium databases were searched for sequences similar to murine FATP1-5 coding regions. Two clones were analyzed in detail; inspection of the entire DNA sequence of these two clones showed that they encode the human orthologs of mmFATP1 and mm FATP4, respectively. These two clones were designated hsFATP1 and hsFATP4, and their
20 DNA and predicted protein sequences are shown in Figures 44A-44C and 45, and 50A-50C and 51. hsFATP1 is predicted to encode a 646 amino acid, 71 kD protein with multiple membrane-spanning domains (Figure 28A). HsFATP4 is predicted to encode a 643 amino acid, 72 kD protein with multiple membrane spanning domains (See Figure 29A). A comparison of the DNA sequences of mouse and human FATP1 and mouse
25 and human FATP4 (Figures 30A-30B and 31A-31B) shows that the mouse and human orthologs are 85% (FATP1) and 87% (FATP4) identical to each other within the coding sequences given in these figures. At the amino acid level, hsFATP1 and hsFATP4 are

66260-4050460

~90% identical to their respective mouse orthologs within the coding region shown in these figures (Figures 32 and 33). The sequence identities between mouse and human FATP1 and FATP4 are considerably higher than the ones observed between different FATP family members within one species (~40%-60%) and are present in the N-terminal part of the protein, a region that is poorly conserved between different FATP family members. This high degree of sequence conservation clearly demonstrates that the newly identified human FATPs are orthologs of mouse FATP1 and FATP4 rather than novel FATP family members.

Table 4 is an identity/similarity matrix comparing the amino acid sequences of FATP1 and 4 from human and mouse. This shows that the gene whose sequence is shown in Figure 43A is indeed human FATP4, since it is 91% identical with the murine FATP4 but only 62% identical with the closest related human FATP, which is FATP1.

Table 4				
Identity/Similarity Matrix				
	hsFATP4	mmFATP4	hsFATP1	mmFATP1
hsFATP4	---	93.2	72.3	72.0
mmFATP4	91.0	---	71.2	71.1
hsFATP1	61.9	61.0	---	92.4
mmFATP1	60.7	59.6	89.5	---

Example 8: Isolation and Sequence Analysis of Full-length Human FATP6

A search of EST databases identified a set of overlapping human sequences that were similar to FATPs, but did not have a clear mouse ortholog. One of these EST clones was found to encode a full-length cDNA. The entire insert of this clone was sequenced and designated hsFATP6. The DNA and predicted protein sequences of hsFATP6 are shown in Figures 54A-54C and 55. HsFATP6 is predicted to encode a 619 amino acid, 70 kD protein with multiple membrane-spanning domains (Figure

35A). A comparison of the amino acid sequences of hsFATP6 with other human FATPs shows about 37% identity to either hsFATP1 or hsFATP4 (Figure 36). This degree of sequence identity is similar to what is observed between different mouse FATPs. The phylogenetic analysis described above clearly demonstrates that hsFATP6 is a member of the FATP family, but not an ortholog of any of the mouse FATPs. Comparisons were done with "ALIGN" (E. Myers and W. Miller, "Optimal Alignments in Linear Space," *CABIOS* 4:11-17 (1988) using standard settings.

Example 9: Tissue Distribution of Human FATPs

The tissue distribution of human FATPs was assessed by Northern blotting.

Human FATP3 was expressed in a large variety of tissues. In contrast, human FATP5 was present at high levels in the liver, but was undetectable in all other tissues examined. Thus, both hsFATP3 and hsFATP5 recapitulate the expression pattern of their mouse orthologs (see above). HsFATP6 is a novel FATP with no mouse ortholog as yet. Northern blotting shows that hsFATP6 is expressed at high levels in the heart, but is undetectable in other tissues, including skeletal and smooth muscle. This tissue distribution suggests that human FATP6 performs an important role in energy metabolism in the heart; blocking FATP6-mediated fatty acid transport may therefore be beneficial for a number of heart diseases, e.g., ischemic heart disease.

To identify the major FATP expressed in the human small intestine, Northern blotting was performed on a blot containing mRNA from human stomach, jejunum, ileum, colon, rectum and lung. hsFATP5 and hsFATP6 were undetectable in any of these tissues. FATP5 is only expressed in liver and FATP6 only in heart. hsFATP2 was weakly expressed in the colon, and an even weaker signal was detectable in jejunum, ileum and lung lanes. hsFATP3 was expressed well in the lung, but was only weakly expressed in the other tissues tested. Importantly, no difference was seen in the expression of hsFATP3 between small intestine and stomach or colon, suggesting that the expression observed is not related to fatty acid absorption in the small intestine. hsFATP4 was clearly expressed in both jejunum and ileum; expression was

significantly lower in the colon and was absent in the stomach. This expression pattern is consistent with a major role for FATP4 in absorption of fatty acids in the human gut.

Example 10: Expression of hsFATP1 and hsFATP4 Promotes Transport of Fatty Acids

COS cells were cotransfected using lipofectamine with the mammalian
5 expression vector pCDNA-CD2 in combination with one of the FATP-containing
expression vectors (pMET7-hsFATP1 or pMET7-hsFATP4) or an insertless expression
vector (pMET7, control) as described in Materials and Methods for Examples 6-10.
COS cells were gated on forward scatter and side scatter. Cells exhibiting more than
400 CD2 fluorescence units representing ~30% of all cells were deemed CD2-positive.
10 The percent of CD2-positive cells exhibiting a BODIPY-fluorescence of >300 is plotted
for the three different vectors tested (Figure 37).

Example 11: Stable Expression of Human FATP4 in 293 Cells

Stable cell lines were generated as follows. A DNA fragment containing the
entire hsFATP4 coding sequence as well as 100 nucleotides of 5' and 50 nucleotides of
15 3' untranslated region was inserted into the vector pIRES-neo (Clontech) using standard
cloning techniques. The resulting construct or a vector control (pIRES-neo) was
transfected into 293 cells using the lipofectamine method (Gibco BRL) according to the
manufacturer's directions. Cells that had taken up the DNA were selected with 1 mg/ml
G418 (Gibco BRL). Single colonies were picked 1 to 2 weeks after transfection and
20 grown in medium containing 0.8 mg/ml G418. Colonies were screened for the ability to
take up fatty acids by measuring uptake of a fluorescently labeled fatty acid (BODIPY-
FA). About 40 colonies transfected with the pIRES-neo containing FATP4 and ~20
colonies transfected with pIRES-neo control were analyzed. All 20 of the vector control
clones showed amounts of BODIFY-FA uptake similar to each other and to
25 untransfected 293 cells. In contrast, among the 40 FATP4 transfected clones, 3 had a 5-
to 10-fold increased BODIPY-FA uptake compared to any of the vector controls, and a
large number (~20) showed an approximately two-fold increase in BODIPY-FA levels.

This distribution is consistent with FATP4 conferring increased fatty acid uptake in these cells. One of the cell lines with the highest amount of BODIPY-FA uptake was selected to be used for measuring uptake of tritiated fatty acid.

The uptake of tritiated oleate over time by either FATP4 expressing or control
5 cells was assayed over time. Expression of FATP4 increases the rate of fatty acid uptake by over 3-fold, demonstrating that FATP4 is, like the other FATPs, a functional fatty acid transporter (Figure 38).

Example 12: Immuno-staining with FATP4-Specific Antiserum

A polyclonal antiserum against the C-terminus of mmFATP4 was raised using a
10 GST-fusion protein having mmFATP4-specific amino acid sequence 552-643 (AVASP...GEEKL). In western blot experiments, the purified antibody reacted strongly with a synthetic peptide matching the C-terminus of mmFATP4, but not with a corresponding region of mmFATP2, mmFATP3, or mmFATP5. The mmFATP4 specific polyclonal antiserum detects, in western blot experiments with enterocyte
15 lysates from 3 different mice, a ~70 kDa protein, which is in accordance with mmFATP4's predicted molecular weight of 72 kDa. The binding is specific for mmFATP4, since it can be completely abolished by preincubation of the antiserum with the GST-fusion peptide used to raise the antibody.

Immunofluorescence experiments were performed using the anti-mmFATP4
20 antiserum on fresh frozen sections of murine small intestine. The antibody binding demonstrates strong expression of mmFATP4 in enterocytes, confirming the results of the in situ hybridization experiments. At higher magnifications it is apparent that mmFATP4 is expressed at the apical side of the enterocyte, indicating that the transporter is present in the brush border membrane, which is known to mediate the
25 uptake of fatty acids from the intestinal lumen.

Immuno-electron microscopy studies were performed on fresh frozen murine intestinal cells. The gold particles used, appearing as black specks on the electron micrographs, indicate the subcellular localization of mmFATP4 to be on the microvilli

of the enterocyte. It can be seen from electron micrographs that mmFATP4 is localized exclusively in membranes, preferentially the apical plasma membrane, confirming that it is indeed a membrane protein.

Methods for Immunofluorescence and Immunogold Electron Microscopy

5 Unfixed mouse small intestine was washed with Hank's buffered salt solution containing 1 mM EDTA, infused with 2.3 M sucrose solution, and embedded in O.C.T., 4583 compound. The material was thick sectioned (15 μ M - 40 μ M). The sections were washed in PBS containing 1% BSA and 0.075% glycine to block non-specific binding. Primary and secondary antibodies were diluted in PBS with 10% FCS and
10 incubated for 1h. The sections were mounted in 90% glycerol/PBS containing 1 mg/ml paraphenylenediamine, and examined with a Bio-Rad MRC 600 confocal, mounted on a Zeiss Axioscop.

 For the immunogold labeling, the tissue was fixed with 2% paraformaldehyde in PBS for 10 minutes, after which it was cryoprotected by infiltration with 2.3 M sucrose
15 in 0.1 M phosphate buffer (pH 7.4) containing 20% polyvinylpyrrolidone, and then mounted on aluminum cryo nails and frozen in liquid nitrogen (Tokuyasu, K.T., *J. Microscop.* 143:139-149, 1986). Ultrathin sections were collected on carbon/formvar-coated nickel grids. The primary antibody (anti-FATP4) was diluted in 10% FCS in PBS and incubated overnight at 4 C, followed by donkey anti-rabbit IgG-gold (12 nm)
20 (Jackson Labs) for 1h. The sections were stained in 2% neutral uranyl acetate (20 minutes) and absorption stained with 2% uranyl acetate in 0.2% methylcellulose containing 3.2% polyvinyl alcohol. The sections were examined with a Philips EM 410 electron microscope.

Example 13: Inhibition of Fatty Acid Uptake Specific to FATP4 Demonstrated in

25 Isolated Mouse Enterocytes

 Phosphorothioate derivatives of the following oligonucleotides were synthesized:

FATP4-AS2	CCCCCACCAGAGAGGCTCC (SEQ ID NO:103)
FATP4-AS2MM	CCACCCCCGGAAAGCCTGC (SEQ ID NO:104)
FATP4-S2	GGAGCCTCTCTGGTGGGGG (SEQ ID NO:105)

5 FATP4 AS2 is the antisense oligo; it is designed to be complementary to the sequence extending from nucleotide 10 to nucleotide 28 of the mouse FATP4 coding sequence. FATP4-AS2MM is a control oligo; in the oligo every third nucleotide was changed creating mismatches; the overall nucleotide composition is identical to FATP4-AS2 (same number of G, A, T, C). FATP4-S2 is the sense control.

10 Enterocytes were isolated from the small intestine of mice and incubated for 48h in tissue culture (Figure 40) either without oligonucleotides (squares) or with 100 μ M FATP4 specific sense (circles) or antisense (diamonds) oligonucleotides. The uptake over time of 25 μ M oleate was then measured. While the FATP4 sense oligonucleotide did not significantly influence the uptake, the antisense oligonucleotide inhibited fatty acid uptake by ~50%.

15 The effect of either FATP4 sense, antisense or mismatch sequence oligonucleotides on the uptake of fatty acids was measured in enterocytes. Isolated enterocytes were incubated with increasing concentrations of FATP4 antisense oligonucleotides (solid bars in Figure 41), or a mismatch control oligonucleotide with identical nucleotide composition (stippled bars), or with 100 μ M of the FATP4 sense-oligonucleotide (lined bar). The medium for this incubation was Dulbecco's modified Eagle's medium with 4.5 g/L glucose, 1 mM sodium pyruvate, 0.01 mg/ml human transferrin and 10% fetal bovine serum. After 48 hours of incubation the uptake of oleate by enterocytes was measured over a 5 minute time interval. Measurements were done in quadruplicate. The uptake assay was done in Hank's buffered salt solution with 20 10 mM taurocholate. Only the enterocytes given FATP4 antisense oligonucleotide showed a concentration dependent decrease of fatty acid uptake, inhibiting it at a 100 μ M concentration by ~50%. This effect was FATP4 specific, since only the antisense oligonucleotide which can bind to the FATP4 mRNA and block its translation inhibited

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uptake, but not a control oligonucleotide differing only in the sequence but not the nucleotide content, ruling out a toxic or otherwise nonspecific inhibitory effect of this oligonucleotide due to its chemical composition.

As a further control experiment, the uptake of oleate was measured along with the uptake of methionine in the same cultured enterocytes. Antisense oligonucleotide, mismatch sequence oligonucleotide, or no oligonucleotide was added to a concentration of 100 μ M to cultures of enterocytes. After incubation for 48 hours, the uptake of both 3 H-labeled oleate and 35 S-labeled methionine was assayed. Results are shown in Figure 42. Fatty acid uptake is at the left side of the paired bars; methionine uptake is on the right side of the paired bars. The fact that amino acid uptake was not influenced by the antisense oligonucleotide treatment further supports the conclusion that the antisense oligonucleotide causes a specific reduction in translation of FATP4-specific mRNA.

Example 14: mmFATP2 Is Expressed in Proximal Renal Tubule Epithelium

Northern analysis showed that mmFATP1, mmFATP2, and mmFATP4 are present in the kidney. In situ hybridization (methods as for Example 6) was performed to determine which cell type(s) of the kidney these mRNAs are expressed in. mmFATP1 mRNA was present in virtually all cells throughout the kidney with no obvious preference for a particular cell type. In contrast, mmFATP2 was expressed only in the renal cortex. Within the cortex, expression of mmFATP2 was restricted to the epithelial cells of the proximal renal tubules. The primary function of proximal renal tubule cells is the reabsorption of filtered salts and nutrients (e.g., glucose), a process that requires mitochondrial oxidation and that can utilize fatty acids as energy substrates. Based on the localization of mmFATP2, it is possible that mmFATP2 is important for reabsorption in the kidney by allowing uptake of an energy source (fatty acids) from the blood into renal epithelial cells. Alternatively, if fatty acids need to be reabsorbed in the kidney, similarly to glucose, FATP2 could be involved in the reabsorption of fatty acids. Determination of the subcellular localization of FATP2 will distinguish between these two possibilities.

Table 5. Mouse FATP mRNA Expression

Mouse Probes	mFATP1	mFATP2	mFATP3	mFATP4	mFATP5
E18.5 embryo expression	everywhere, brain = thymus> heart> brown fat, others	liver (hepatocytes)	-	Brain, small intestine, superior cervical ganglion (SCG), dorsal root ganglion (DRG), other regions have lower expression	Mouse Probes
Duodenum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Jejunum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Ileum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Colon	low expression in the crypt	very low level in the crypt	-	-	-
Kidney	cortex and medulla	proximal tubules	-	-	-

Table 5 (continued). Mouse FATP mRNA Expression

Mouse Probes	mFATP1	mFATP2	mFATP3	mFATP4	mFATP5
Liver	-	hepatocytes	hepatocytes	-	hepatocytes
Pancreas	exocrine secretory units or acinar cells; endocrine pancreas (islet) are negative	exocrine secretory units or acinar cells; endocrine pancreas (islet) are negative	-	-	-
Brain	Neuronal expression throughout the brain including hypothalamus	-	-	Neuronal expression throughout the brain including hypothalamus	-
Heart	myocytes	-	-		
Testis	seminiferous tubules	-	seminiferous tubules		
Lung	bronchiole	-	-		
Adipose	adipocyte	adipocyte	-		

Example 15: Isolation of full-length human FATP3

Full-length clones encoding human FATP3 were identified by searching databases for sequences similar to the murine FATP1-5 coding regions using the BlastX algorithm (Altschul *et al.*, *J. Mol. Biol.* 215: 403-410, 1990). Human clones with

5 similarity to the 5' end of murine FATP sequences were sequenced completely. A clone encoding full-length human FATP3 was obtained from a human bone library constructed in the mammalian expression vector pMET7 (Tartaglia, L.A. *et al.*, *Cell* 83: 1263-1271, 1995). To identify human cDNA clones encoding FATP family members, databases were searched for sequences similar to murine FATP1-5 coding regions. One

10 clone was found to encode the human ortholog of mmFATP3 and was designated hsFATP3. The DNA and predicted protein sequences of hsFATP3 are shown in Figures 94A and 94B. hsFATP5 is predicted to encode a 703 amino acid 75.6 kD protein with multiple membrane-spanning domains. A comparison of the DNA sequences of mouse and human FATP3 shows that the mouse and human orthologs are 81% identical to

15 each other within the coding region. At the amino acid level, hsFATP3 is ~86% identical to mm FATP3 within the coding region. The sequence identities between mouse and human FATP3 are considerably higher than those observed between different FATP family members within one species (~40%) and are present in the N-terminal part of the protein, a region that is poorly conserved between different FATP

20 family members.

Example 16: Substrate Specificity of Fatty Acid Transport in hsFATP-Transfected Clones

Using a mammalian expression vector, we generated 40 stable 239 cell lines expressing hsFATP4 and 20 cell lines transfected with a control plasmid. The ability of

25 the different cell lines to take up FA, as assessed by uptake assays using the fluorescently labeled Bodipy-palmitate, correlated well with their FATP4 expression levels determined by Western blotting (FIG. 95). All 20 vector control clones showed amounts of Bodipy-FA uptake similar to each other and to untransfected 239 cells. In contrast, among the 40 FATP4 transfected clones, a large number (~20) showed an

approximately 2-fold increase in Bodipy-FA uptake compared to any of the vector controls, and three had a 5- to 10-fold increase in Bodipy-FA uptake.

Several of the cell lines with the highest amount of Bodipy-FA uptake as well as isolated primary enterocytes were used to measure the uptake of radiolabeled FAs.

- 5 Short-term uptake by 293 cells and enterocytes of all FAs tested was linear (FIG. 97). hsFATP4 expression enhanced the rate of palmitate uptake approximately 3 fold over 293 cells transfected with vector alone (FIG. 97) and also accelerated the uptake of oleate but not of linolate, arachidonate, octanoate, butyrate or cholesterol (Table 6). Isolated primary enterocytes showed a similar preference for palmitate and oleate, and
- 10 absence of transport of arachidonate, octanoate, and butyrate, but displayed a more robust transport of linolate and cholesterol than the transfected 293 cells.

- To further characterize the substrate specificity of FATP4, we measured the uptake by stably transfected 293 cells of 5 μ M Bodipy-FA in the presence of a 20 fold molar excess (i.e., 100 μ M) of FAs, FA-derivatives and lipid soluble vitamins and
- 15 hormones. Both saturated and non-saturated fatty acids containing 10 to 26 C atoms strongly competed for uptake of Bodipy-palmitate (FIG. 96 and Table 7) and thus are presumed to be substrates of FATP4. In contrast, fatty acids with eight or fewer C atoms did not compete and thus are presumed not to be FATP4 substrates. Similarly, esters of long chain FAs and other hydrophobic molecules tested had no effect on
- 20 uptake of Bodipy-palmitate.

LCFA Uptake Assays (Methods)

- Bodipy-FA uptake assays using FACS were performed, adapted to a 96-well format. LCFA uptake assays with enterocytes or with stably transfected 293 cells were done as follows. Mixed micelles of radiolabeled FA (NEN) and taurocholate (Sigma) in
- 25 HBS were generated by brief sonication at 37°C. Equal volumes of cells and micelle solution were mixed, resulting in a final FA concentration of 25 μ M for antisense assays and 10 μ M for substrate specificity assays. Final taurocholate concentration was 5 mM. Cells were incubated for the indicated amount of time at 37°C. The assay was stopped by transferring the cells onto filter paper followed by extensive washes with

[illegible]

Table 6
Uptake of Different Substrates by FATP4 Expressing Cell Lines and Enterocytes

Fatty Acid	293 Cells Control*	293 Cells Stably Expressing FATP4	FATP4 specific	Enterocytes*
Palmitate	564	1695	1131	3036
Oleate	662	1122	459	117
Linolate	640	673	33	116
Arachidonate	3	5	2	0
Octanoate	0	0	0	5
Butyrate	0	50	50	73
Cholesterol	319	345	26	531

Uptake of different substrates by enterocytes and by control and stable FATP4-expressing 293 cells. The rates of uptake for the indicated fatty acids was measured over 4 min taking measurements every 30 s. All fatty acids were at a concentration of 10 µM in HBS containing 5 mM taurocholate.

*Uptake measured as *pmol/min 10⁶ cells*

Table 7

Competition of Bodipy-FA Uptake by FATP4 Expressing Cells

Fatty Acids	Formula	Competition
Butyric Acid	$C_4H_8O_2$	-
Caproic Acid	$C_6H_{12}O_2$	-
Caprylic Acid	$C_8H_{16}O_2$	-
Capric Acid	$C_{10}H_{20}O_2$	++
Lauric Acid	$C_{12}H_{24}O_2$	++
Myristic Acid	$C_{14}H_{28}O_2$	++
Palmitic Acid	$C_{16}H_{32}O_2$	++
Stearic Acid	$C_{18}H_{36}O_2$	+
Oleic Acid	$C_{18}H_{34}O_2$	++
Linoleic Acid	$C_{18}H_{32}O_2$	++
Arachidic Acid	$C_{20}H_{40}O_2$	++
Lignoceric Acid	$C_{24}H_{48}O_2$	++
Cerotic Acid	$C_{26}H_{52}O_2$	++

Fatty Acid Derivatives

Fatty Acids	Formula	Competition
Palmitic Acid Methyl Ester	$C_{17}H_{34}O_2$	-
Stearic Acid Methyl Ester	$C_{19}H_{38}O_2$	-
Oleic Acid Ethyl Ester	$C_{20}H_{38}O_2$	-
Oleic Acid Oley Ester	$C_{36}H_{68}O_2$	-
Oleoyl CoA	$C_{39}H_{68}N_7O_{17}P_3S$	-
Cholesteryl Oleate	$C_{45}H_{78}O_2$	-

Table 7 Continued
Competition of Bodipy-FA Uptake by FATP4 Expressing Cells

Lipid-Soluble Vitamins & Homones

Fatty Acids	Formula	Competition
Retinoic Acid (Pro-Vitamin A)	C ₂₀ H ₂₈ O ₂	±
Ergocalciferol (Vitamin D2)	C ₂₈ H ₄₄ O ₂	-
Tocopherol (Vitamin E)	C ₂₉ H ₅₀ O ₂	-
3-Phytylamenadione (Vitamin K1)	C ₃₁ H ₄₆ O ₂	-
Prostaglandin E2	C ₂₀ H ₃₂ O ₅	-

Competition for Bodipy-FA uptake by FATP4 expressing cells by different hydrophobic compounds. The uptake of 5 µM Bodipy-FA, C1-Bodipy-C12 was measured in the presence of a 20-fold molar excess (i.e., 100 µM) of the indicated fatty acids or fatty acid derivatives. The maximal 100% inhibition was defined as the amount of Bodipy-FA incorporated in the presence of 200 µM lauric acid which was on average 18% ± 5% that of untreated cells.

- : 0% - 30% inhibition by the indicated substance
- ±: 30% - 50% inhibition
- +: 50% - 70% inhibition
- ++: 70% - 100% inhibition

All references cited herein are incorporated by reference in their entirety.

While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention as defined by the appended claims.

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CLAIMS

What is claimed is:

1. A method for identifying an agent which binds to a protein comprising an amino acid sequence of SEQ ID NO:49 or SEQ ID NO:53, comprising the steps of
5 contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
2. The method of Claim 1 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
- 10 3. The method of Claim 1 wherein the isolated protein is in isolated plasma membrane.
4. A method for identifying an agent which inhibits interaction between an isolated protein comprising amino acid sequence SEQ ID NO:49, or SEQ ID NO:53, and further comprising a ligand of said protein, comprising:
15 (a) combining:
 - (1) said isolated protein;
 - (2) the ligand of said protein; and
 - (3) a candidate agent to be assessed for its ability to inhibit
20 interaction between said protein of (1) and the ligand of (2),
under conditions appropriate for interaction between the said
protein of (1) and the ligand of (2);
- (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which
25 interaction of said protein of (1) and the ligand of (2) occurs in the

absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);

wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

- 5 5. The method of Claim 4 wherein (a) is performed in an artificial membrane system.
- 10 6. The method of Claim 4 wherein said isolated protein is in isolated plasma membrane.
- 15 7. A method for identifying an agent which binds to a protein, said protein encoded by (1) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions, or by (2) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
- 20 8. The method of Claim 7 wherein the step of contacting the agent with the isolated protein is performed in an artificial membrane system.
- 25

9. The method of Claim 7 wherein the isolated protein is in isolated plasma membrane.
10. A method for identifying an agent which inhibits interaction between (1) an isolated protein, said protein being encoded by (i) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions, or by (ii) a polynucleotide having a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions and (2) a ligand of said protein, comprising:
- (a) combining:
 - (1) said isolated protein;
 - (2) the ligand of said protein; and
 - (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between said protein of (1) and the ligand of (2);
 - (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
 - (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the

candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

11. The method of Claim 10 wherein (a) is performed in an artificial membrane system.
- 5 12. The method of Claim 10 wherein said isolated protein is in isolated plasma membrane.
- 10 13. A method for identifying an agent which binds to a protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49, or SEQ ID NO:53 comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
- 15 14. The method of Claim 13 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
15. The method of Claim 13 wherein the isolated protein is in isolated plasma membrane.
- 20 16. A method for identifying an agent which inhibits interaction between (i) an isolated protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49, or (ii) a protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid

sequence similarity with the amino acid sequence in SEQ ID NO:53 and a ligand of said protein, said method comprising:

(a) combining:

- (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);

(b) determining the extent to which said protein of (1) and the ligand of (2) interact; and

(c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);

wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

17. The method of Claim 16 wherein (a) is performed in an artificial membrane system.

18. The method of Claim 16 wherein said isolated protein is in isolated plasma membrane.

19. A method for identifying an agent which is an inhibitor of fatty acid uptake by (i) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID

NO:49, or by (ii) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- 5 a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

10 wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.

20. An inhibitor of fatty acid uptake identified by the method of Claim 19.

21. The method of Claim 19 further comprising the steps of:

- 15 a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
- d) comparing the fatty acids of b) with the fatty acids of c);

20 whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

22. An inhibitor of fatty acid uptake identified by the method of Claim 21.

23. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein encoded by (i) a polynucleotide comprising a nucleotide
25 sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide

hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions, or by (ii) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.

24. An inhibitor of fatty acid uptake identified by the method of Claim 23.

25. The method of Claim 23 further comprising the steps of:

- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
- d) comparing the fatty acids of b) with the fatty acids of c);

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

26. An inhibitor of fatty acid uptake identified by the method of Claim 25.

27. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein being encoded by (i) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49 or by (ii) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and
 - c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
28. An inhibitor of fatty acid uptake identified by the method of Claim 27.
29. The method of Claim 27 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
30. An inhibitor of fatty acid uptake identified by the method of Claim 27.

31. A method for identifying an agent which is an inhibitor of (i) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:49 or (ii) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:53, comprising the steps of:
- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- 10 (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to
- 15 the second aliquot is indicative that the agent is an inhibitor of said protein.
32. The method of Claim 31 further comprising the steps of:
- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- 20 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 25 33. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by (i) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a

complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions, or by (ii) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of:

- (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

34. The method of Claim 33 further comprising the steps of:

- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c);

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

35. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by (i) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid

sequence similarity with the amino acid sequence in SEQ ID NO:49 or by (ii) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of
10 said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

- 15 36. The method of Claim 35 further comprising the steps of:
 - a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable
20 samples of tissue or bodily fluid from suitable control animals; and
 - d) comparing the fatty acids of b) with the fatty acids of c).

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

- 25 37. A method for identifying an agent which binds to a protein comprising an amino acid sequence of SEQ ID NO:57, comprising the steps of contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

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38. The method of Claim 37 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
39. The method of Claim 37 wherein the isolated protein is in isolated plasma membrane.
- 5 40. A method for identifying an agent which inhibits interaction between an isolated protein comprising an amino acid sequence of SEQ ID NO:57, and further comprising a ligand of said protein, comprising:
- 10 (a) combining:
- (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- 15 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 20 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 25 between said protein and the ligand of said protein.
41. The method of Claim 40 wherein (a) is performed in an artificial membrane system.

42. The method of Claim 40 wherein said isolated protein is in isolated plasma membrane.
43. A method for identifying an agent which binds to a protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
44. The method of Claim 43 wherein the step of contacting the agent with the isolated protein is performed in an artificial membrane system.
45. The method of Claim 43 wherein the isolated protein is in isolated plasma membrane.
46. A method for identifying an agent which inhibits interaction between (1) an isolated protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, and (2) a ligand of said protein, comprising:
- (a) combining:
 - (1) said isolated protein;
 - (2) the ligand of said protein; and
 - (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2),

under conditions appropriate for interaction between said protein of (1) and the ligand of (2);

- (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);

wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

47. The method of Claim 46 wherein (a) is performed in an artificial membrane system.
48. The method of Claim 46 wherein the isolated protein is in isolated plasma membrane.
49. A method for identifying an agent which binds to a protein encoded by a nucleic acid encoding a fatty acid transport protein consisting of an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57 comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
50. The method of Claim 49 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.

51. The method of Claim 49 wherein the isolated protein is in isolated plasma membrane.

52. A method for identifying an agent which inhibits interaction between an isolated protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57 and a ligand of said protein, said method comprising:

(a) combining:

(1) said isolated protein;

(2) the ligand of said protein; and

(3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);

(b) determining the extent to which said protein of (1) and the ligand of (2) interact; and

(c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);

wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

53. The method of Claim 52 wherein (a) is performed in an artificial membrane system.

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54. The method of Claim 52 wherein said isolated protein is in isolated plasma membrane.
55. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID NO:57, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and
 - c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
56. An inhibitor of fatty acid uptake identified by the method of Claim 55.
57. The method of Claim 55 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
58. An inhibitor of fatty acid uptake identified by the method of Claim 57.

59. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and
 - c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
60. An inhibitor of fatty acid uptake identified by the method of Claim 59.
61. The method of Claim 59 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
62. An inhibitor of fatty acid uptake identified by the method of Claim 61.

63. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein being encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57, comprising the steps of:
- 5
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
 - b) measuring uptake of the fatty acid in the test cells; and
 - c) comparing uptake of the fatty acid in the test cells with uptake of the
- 10 fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
64. An inhibitor of fatty acid uptake identified by the method of Claim 63.
- 15 65. The method of Claim 63 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable
- 20 samples of tissue or bodily fluid from suitable control animals;
- d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
66. An inhibitor of fatty acid uptake identified by the method of Claim 65.

67. A method for identifying an agent which is an inhibitor of a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:57, comprising the steps of:
- (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
 - (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
 - (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
 - (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.
68. The method of Claim 67 further comprising the steps of:
- a) administering the agent to one or more test animals;
 - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
 - c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
 - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
69. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of:

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- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

10 wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

70. The method of Claim 69 further comprising the steps of:

- 15 a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

20 71. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence homology with the amino acid sequence in SEQ ID NO:57, comprising the steps of:

- 25 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;

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- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

5 wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

72. The method of Claim 71 further comprising the steps of:

- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c).

10

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

15

73. A method for identifying an agent which is an inhibitor of a fatty acid transport protein, comprising the steps of:

- (a) introducing into cells one or more vectors comprising a gene encoding a cell surface protein and a nucleic acid encoding the fatty acid transport protein;
- (b) contacting the host cells with anti-cell surface protein antibody and labeled fatty acid substrate of the fatty acid transport protein;
- (c) contacting a first aliquot of the host cells with an agent being tested as an inhibitor of the fatty acid transport protein, while leaving a second aliquot of the host cells uncontacted with the agent;
- (d) identifying, in the first and second aliquots, the host cells expressing the cell surface protein by detecting the anti-cell surface protein antibody bound to the host cells; and

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- (e) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells identified as expressing the cell surface protein;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of the fatty acid transport protein.

74. The method of Claim 73 wherein the host cells regulably express the FATP4 gene.

75. The method of Claim 73 wherein the host cells are prokaryotes.

76. The method of Claim 73 wherein the prokaryotes are *E. coli*.

77. The method of Claim 73 wherein the fatty acid is a radioactively labeled fatty acid.

78. A method for identifying an agent which is an inhibitor of FATP4, comprising the steps of:

- (a) introducing into cells one or more vectors comprising a gene encoding a cell surface protein and a nucleic acid encoding FATP4;
- (b) contacting the host cells with anti-cell surface protein antibody and labeled fatty acid substrate of FATP4;
- (c) contacting a first aliquot of the host cells with an agent being tested as an inhibitor of FATP4, while leaving a second aliquot of the host cells uncontacted with the agent;
- (d) identifying, in the first and second aliquots, the host cells expressing the cell surface protein by detecting the anti-cell surface protein antibody bound to the host cells; and

- (e) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells identified as expressing the cell surface protein;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of FATP4.

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79. The method of Claim 78 further comprising the steps of:

- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c);

10

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

15 80. The method of Claim 78 wherein the cell surface protein is CD2.

81. The method of Claim 78 wherein the fatty acid substrate is BODIPY-labeled.

FATTY ACID TRANSPORT PROTEINS

ABSTRACT OF THE DISCLOSURE

A family of fatty acid transport proteins (FATPs) mediate transport of long chain fatty acids (LCFAs) across cell membranes into cells. These proteins exhibit different expression patterns among the organs of mammals. Nucleic acids encoding FATPs of this family, vectors comprising these nucleic acids, as well as the production of FATP proteins in host cells are described. Also described are methods to test FATPs for fatty acid transport function, and methods to identify inhibitors or enhancers of transport function. The altering of LCFA uptake by administering to the mammal an inhibitor or enhancer of FATP transport function of a FATP in the small intestine can decrease or increase calories available as fats, and can decrease or increase circulating fatty acids. The organ specificity of FATP distribution can be exploited in methods to direct drugs, diagnostic indicators and so forth to an organ such as the heart.

Fig. 2A

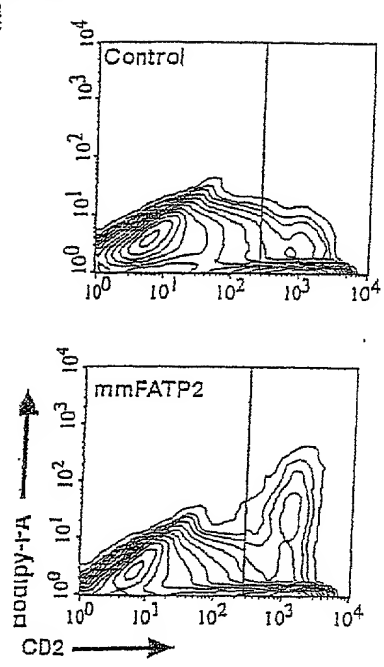


Fig. 2C

Fig. 2B

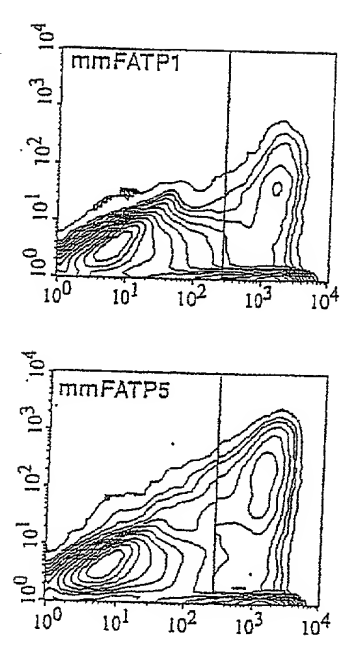


Fig. 2D

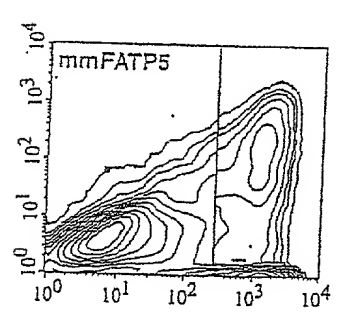


Fig. 3

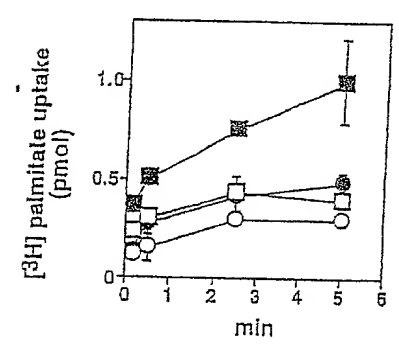
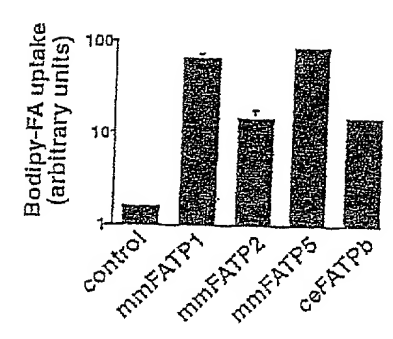


Fig. 4

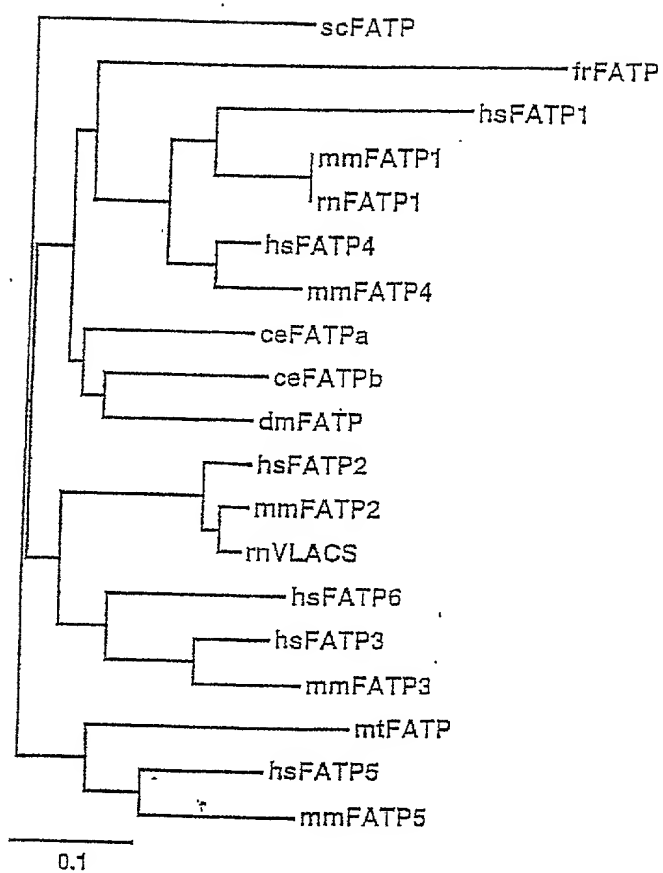


Figure 5

FIG. 6

246	FTTSGTGTGPKPAILSHERVIOVSNVLSFCGCR--	ADDVVYDVLP	LYHTIGLVGLGCLQV	GATCVIAPKFSASRFAEGRQHGVIVV	mmFATP1				
265	VIVTSGITGNPKPAVIAIKHFRFWI--	AMGAKAFGINKSDVYIT	MPMYHSAAGMGTGSLIAF	GSTAVIRKKFSASNWKDCVKVNVITAT	mmFATP5				
249	-IVTSGITGDKSAHNSWRKSSVGCQVFG-	HVHMTNESTVFTAMP	FEHSTAALGACALSHGCL	ALSHKFSASTENKQVYLTGNTHH	cefATPa				
256	YIVTSGITGDKPAAIVVSRYYR-	AAEGHHSYSMRAADV	LDCPLVYHSAAGNMGVQC	VIYELHVVERKKFSASREWDDGVKYNCTVV	scFATP				
205	XIVTSGITGDKPAAIVVSRYYR-	AAEGHHSYSMRAADV	LDCPLVYHSAAGNMGVQC	VIYELHVVERKKFSASREWDDGVKYNCTVV	mtFATP				
205	XIVTSGITGDKPAAIVVSRYYR-	AAEGHHSYSMRAADV	LDCPLVYHSAAGNMGVQC	VIYELHVVERKKFSASREWDDGVKYNCTVV	mtFATP				
100	110	120	130	140	150	160	170	180	
335	OYVIGETICRYLROBPVRDVFORHVR-	AVNGNLRPAIWEFF	TQREHGVPOIGEFYCAT	EC--	NCSLANMDCKVSGSGGNSRRLTHV--	VP	mmFATP1		
353	LAVGEJLRVHCNVPEQPEDKIHIVRL	AMCTELRANVWKNFQORE	GPRIWEFYGSTEG--	NVGLMNY--	VGHGGAAGRTSCILRMETP	mmFATP5			
338	OYVIGETICRYLROBPVRDVFORHVR-	AVNGNLRPAIWEFF	TQREHGVPOIGEFYCAT	EC--	NCSLANMDCKVSGSGGNSRRLTHV--	VP	mmFATP1		
345	OYVIGETICRYLROBPVRDVFORHVR-	AVNGNLRPAIWEFF	TQREHGVPOIGEFYCAT	EC--	NCSLANMDCKVSGSGGNSRRLTHV--	VP	mmFATP1		
295	VYVIGETICRYLROBPVRDVFORHVR-	AVNGNLRPAIWEFF	TQREHGVPOIGEFYCAT	EC--	NCSLANMDCKVSGSGGNSRRLTHV--	VP	mmFATP1		
190	200	210	220	230	240	250	260	270	
419	IRLVKVNEDTMEPT-RDSEGLCIEPCQ	GEPLGLVGOIN-QQDELRREDGVV-	SDSATNRKKAHSVFRKGE	DSAYLISGDVIVMDEEGYMYER	mmFATP1				
437	FELVQFQIETAEPL-RBKQGFCTP	VEPGKPGLLTKVR-KNOP--	ELGVRSQAESNRKLVANVR	RVGDBLYENTGDMVTLDDQEGFF	mmFATP5				
424	VRLIKVDRAATGELE-RDKNGLCVP	CVRGHETGEMVGVIK-EKDI	ILKTEGVV-SEGDTAKKIYR	GVFKHGDVKAASGDIHWDDEGLVYFV	cefATPa				
434	QTLVRMDPNDDSVIYRNSKGFGE	VAPVGEPPGEMLMKILFFPK	PETSFQGYLGNAKETKSKVVR	RDVRRGDWYRCGBLLKADBYGLNML	scFATP				
373	LAFVEYDLDTGDEL-RDASGRVRR	VPDGEPLLSRVN-RLQP--	EDGYTDP-VASEKKLVRNA	FRDGCWENTGDMSPQGMGHAAFY	mtFATP				
280	290	300	310	320	330	340	350	360	
506	DRSGDTERWRGENVSTTEVEAVLSR	LLGQT--	DVAVYGVAVPGVEGKAGMAA	IADPHS--	QLDP--	NSMYQELQK-VIASVAR	mmFATP1		
522	DRSGDTERWRGENVSTTEVEAVLSR	LLGQT--	DVAVYGVAVPGVEGKAGMAA	IADPHS--	QLDP--	NSMYQELQK-VIASVAR	mmFATP1		
511	DRSGDTERWRGENVSTTEVEAVLSR	LLGQT--	DVAVYGVAVPGVEGKAGMAA	IADPHS--	QLDP--	NSMYQELQK-VIASVAR	mmFATP1		
524	DRSGDTERWRGENVSTTEVEAVLSR	LLGQT--	DVAVYGVAVPGVEGKAGMAA	IADPHS--	QLDP--	NSMYQELQK-VIASVAR	mmFATP1		
457	DRSGDTERWRGENVSTTEVEAVLSR	LLGQT--	DVAVYGVAVPGVEGKAGMAA	IADPHS--	QLDP--	NSMYQELQK-VIASVAR	mmFATP1		

66260-4050460

mmFATP3 DNA sequence

ACGACTCACTATAGCGACAGAGCCTATGACGTCCCATGCAC 40
GGGTAAGCTTTGGGCCCCCTCGAGGGATGCTCTAGAGCGGCC 80
GCGGACCCCGAAAGCTCTGACAGCGGGTGCAGTCTGGGCT 120
GGCGTCTCGGTAACCTGGCCCCGGGAGCAGCGGACACACAC 160
CTTCCTCATCCACGGCGCGGACCGGCTTTAGCTACGGCGAG 200
GCTGAGCGCGAGAGCAACCGGATTCCTCGCGGCTTTCTGC 240
GCGCACGGGGGCTGGAACCGGGGGGCGCGGAGGCTCGGGCAG 280
GGGCAGCACTCAGGAAGGCGCAGCGGTGCGGCGCTCGGGCT 320
GGAGATCGGGCTGCTAGAGGGACGACCGGCGCCCCCTCTGG 360
CAACCGGGGGGACCGGTGGCGCTGCTCTCTCCAGCGGGGCC 400

Figure 8A

GCATTTTCCTTTTCGATTITGGHTGGGACTGGGCAAAAGCTGGC 440
 CTGGGCAAGGCTCTTTTGTGGGCAAGGCTTTTACGGGAGGAC 480
 CCGTGGTGGCACTGGCTCCGGAGCTGGGHTGGGAGTGGCT 520
 CGTGGTGGGCAAGAGTTCCTGGAGTCCCTGGAGGCGGAC 560
 CTGGGCGGCTTTGACAGGCAATGGGGCTCCACCTATGGGCGA 600
 CCGGCGCTGAAACTAATGTAGCTGCAATCAGCAATTTGCT 640
 ATGGCAAGCAGCAGACCAAGTGGATGAGGAGTGGGCGG 680
 TACCTCTCTGGGCGGCGACACATAATGGACACCTGGCTGT 720
 ACATCTTTCACCTCTGGGCTACTAGTGGGCTGGGCAAGGCTGC 760
 TCGAATCAGTATCTGCAAGGTTCTACAGTGGGAGGCTATC 800
 TACCATCTGTGTGGAGTCCACAGGAGGAGGCTATCTACC 840
 TGGCACTCCCACTGTACACATGTCTGGCTCCCTTCTGGG 880
 CATTTGGGGCTGGCTGGGCAATGGGGCGACGGTGGGTCTG 920
 AAACCCCAAGTCTCAGCTAGGCAAGTCTGGGAGGATTTGGC 960
 AGAAACACAGGGTACAGTGTTCAGTACATTTGGGAGTT 1000
 GTGGGCAATCCCTGGTCAACAGGCGGCGAGCAAGGCAGAG 1040
 TTGTACCATAGGTTGGGCTGGGAGTGGGAGTGGGTTC 1080
 GGGCAGACACCTGGGAGGCTTCTGGGCGATTTGGAC 1120
 TCTGCAGATACTGGGAGGATGGCATGACAGAGGGCAAC 1160
 GTAGCTACGTTCAATTACACAGGAGGGCAGGGTCCAGTGG 1200
 GGGCAGGCTTCCCTGGGCTTTACAGGACATCTTCCCTTCTC 1240
 CTTCATTCGATACGATGTATGACAGGGGAGGCTATTGG 1280
 AATGCGGAGGGGCACTGCTATGACACATCTCCAGGAGG 1320
 CAGGCGTACTGGTGGGCGGAGTGGGAGGAGTCCGCTT 1360
 CCTGGGCTATGCTGGGCTCCGGAGCTGGGCAAGGACAAG 1400
 CTGCTGAGGATGTCTTCTGGTCTGGGAGGTTTTCTTCA 1440
 ATACTGGGCACTCTHGGTCTGTGATGAGCAAGGCTTTCT 1480
 TCACTTCCAGCATGCTACTGGGAGACACCATCAGGAGGAG 1520
 GGAGAGAAATGTGGGCAAACTGAAGTGGCTGAGGCTTGG 1560
 AGACCGTGGCACTTCCCTCAGGAGGTGAACATCTATGGAGT 1600
 CAGGGTGGCAGGGCAGGAGGAGGAGGAGGAGGAGGAGG 1640
 TTGGCTCTGGGCGGCGGAGGCTCTGAACCTGGTGGAGC 1680
 TCTACAGGCAATGTTTCTGAGAACTTGGCAAGGATGGGCG 1720
 AACTGGGTTTCTCAGGCTCCAGGAATCTTTGGGCACTACT 1760
 GAGACCTTCAAAACAGCAGAGGTTAGGATGGGCAATGAGG 1800
 GCTTTCACCCAGTGTACTGTCTGAGGAGGAGGAGGAGG 1840
 GGAGCAAGATATAGGGGCTACCTGGGCGTCAACCTGGC 1880
 CGGTACAGTGGGCTCTGTCTGGAGACCTTGAATCTGAA 1920
 AACTTCCACTTACAGGAGGGGCTGGAGGAGGAGGAGG 1960
 CATGGCTGACCAAGGAGGAGGTTTTGGGATCTTTTGTAT 2000
 ATGGAGTCATTATTTTGTAAATAAACAGCTGGAGCTTAAA 2040
 AA 2080
 AAAAAA 2087

Figure 8B

mmFATP3 protein sequence

AADPESSSESGCSLAWRLAYLAREQPIHTFLIHGAQRFSYAEAFRESNRIA 50
 RAFLRARGWIGGRRGSGRGSTEHCARVAPPAGDAAARGITAPPLAPGATV 100
 ALLLPAGPDEFWIFGLAKAGLRITAFVPTALRRGPLIHCLRSOGASALVL 150
 ATEFLESLEPDLPALRAMGLHLWATGPEINWAGISNLLSEADQVDEFVP 200
 GYLSAPQNMIDICLYIFTSGITGLPKAARLSHLKVLQCOQFYHLQGVHQE 250
 DVITYALPLYHMSGSLLGIVGCLGIGATVVLKPKFSASQFWDQOKHRVT 300
 VFQYIGELCRYLNNQPPSKAEFDHKVRLAVGSGLRPDIWERFLRRFGPLQ 350
 ILLEYGMTEGNWATFNNTGRQCAVGRASWLYKHLEPFSILRYDVMIGEPI 400
 RNAQGHOMITSPGEFGLIVAFVSQOSPFLGYACAPELAKDKLLKDVFWSG 450
 DVFNIGDLLVCDQGFTHFHRTGDTIRWKGENVATTEVAEVLLEILDFL 500
 QEVNLYGVIVPGHEGFRAGMAALALRPPQALNLVQLYSHVSENLPYARER 550
 FLRLQESLATTEITFKQOKVRMANEGFDPSVLSDPLYVLDQDIGAYLELTP 600
 ARYSALLSGDLRI 613

Figure 9

mmFATP4 DNA sequence

CCCAAGCGTCCGCCCAAGCGTCCGGCATGGCCAAAGCTGGG 40
 CGTGGAGGCGGCTCTCATCAACACCAACCTTAGGCGGGAT 80
 GCGCTGGCCACTGTCTTGACACCTCAAAGGCACGAGCTC 120
 TCATCTTTGGCAGTGAGATGGCCTCAGCTATCTGTGAGAT 160
 CCATGCTAGCCTGGAGGCCACACTCAGCCTCTTCTGCTCT 200
 GGATCCCTGGGAGGCCAGCACAGTGGCCGTCAGCACAGAGC 240
 ATCTGCACCTCTTCTGGAAGATGCCCGAAGCACTTGGC 280
 CAGTCACCCAGACAAGGGTTTTACAGATAAGCTCTTCTAC 320
 ATCTACACATCGGGCACCACGGGGCTACCCAAAGCTGCCA 360
 TTGTGGTGCCACAGCAGGTATTATCGTATGGCTTCCCTGGT 400
 GTACTATGGATTCCGATGCGGCTGATGACATTGTCTAT 440
 GACTGCCCTCCCCCTCTACCACTCAAGCAGGAACATCGTG 480
 GCGATTGGCAGTGTCTACTCCACGGCATGACTGTGGTGAT 520
 CCGGAAGAAGTCTCTAGCCTTCCCGGTTCTGGGATGATTGT 560
 ATCAAGTACAACTGCACAGTGGTACAGTACATTGGGAGC 600
 TCTGCCGCTACCTCTGAACACGCCACCCCGTGAGGCTGA 640
 GTCTGGGCACAAGGTGGCGATGGCACTGGGCAACGGTCTC 680
 CCGCAGTCCATCTGGACGGACTTCTCCAGCCGTTTCCACA 720

Figure 10A

09405504-092399

TCCCCCAGGIGGCTGAGTTCTATGCGGCACTGAATGCAA 760
 CTGTAGCCTCGGCAACTTTGACAGCGGGGCGGGGCTGT 800
 GGCCTCAATAGCCGCATCCTGTCTTTGTTGTAACCTATCC 840
 GTTTGGTACGTGTCAATGAGGATAACCATGCAACTGATCCG 880
 GGGACCCGATGGAGTCTGCAATCCCTGTCAACCAGGTGAG 920
 CCAGGSCAGCTGGTGGGTGGCATCATCCAGCAGGACCCCTC 960
 TGCGCGGTTTCGACGGGTACCTCAACCAGGGTGGCAACAA 1000
 CAAGAAGATTGGCTAATGATGTCTTCAAGAAGGGGGACCAA 1040
 GCTTACCTCACCTGGTGAAGTCTCTGGTGATGATGAGCTGG 1080
 GTTACCTGTACCTCCGAGATCCCACTGGGGACACGTTCCG 1120
 CTGGAAGGGGAGAAATGTATCTTACCACTGAGGTGGAGGGC 1160
 ACACTCAGCCCGCTGCTTCATATGGCAGATGTGGCAGTTT 1200
 ATGGTGTGTGAGGTGGCAGGAAGTGAAGGCGGAGCAGGAAT 1240
 GGCTGCGGTTTGAAGTCCCATCAGCAACTGTGACCTGGAG 1280
 AGCTTTGACAGACCTTTGAAAAAGGAGCTGCTCTGTATG 1320
 CCGGCCCCCATCTTCTGCGCTTCTTGGCTGAGCTGCACAA 1360
 GACAGGGACCTTCAAGTTCCAGAAGACAGAGTTGGCGAAG 1400
 GACGGCTTTGACCCATCTGTGTGTGAAAGACCCGCTGTCT 1440
 ATCTGGATGCTGGGAAGGGCTGCTACGTTGCACTGGACCA 1480
 GGAGGCTATACCCGCATCCAGGCAGGCGAGGAGAAGCTG 1520
 TCATTTTCCCCCTACATCCCTCTGAGGGCCAGAAGATGCTG 1560
 GATTACAGAGCCCTAGCGTCCACCCAGAGGGTCTCTGGCA 1600
 ATGCCAGACCAAAGCTAGCAGGGGCGCGACCTCCGCCCCCT 1640
 AGGTGCTGTATCTCCCTCTCTCCAAACTGCCAAGTACTCA 1680
 CTGCGCGCTTCCCCGACCCCTCCAGAGGCTTTCTGTGAAAGT 1720
 CTCATCCAAGCTGTGTCTTCTGGTCCAGGCGTGGCCCCCTG 1760
 GCCCCAGGGTTTCTGTATAGGCTCCCTTATGATGGTATCTT 1800
 GCGTCCAGCGGGCCAGGGTGTGGGACAGGAGTCACTAAGA 1840
 TCCCTCCAATCAGTAAGGGAGCTTACAAAGGAACCAAGGCA 1880
 AAGCTGTAGACTCAGGAAGCTAAGTGGCCAGAGACTATA 1920
 GTGGCCAGTCACTCCCATGTCCACAGAGGATCTTTGGTCCAG 1960
 AGCTGCCAAAGTGTACCTCTCTCCCTGCTGCACTCTGCGG 2000
 GAAAAGAGGACAGCATGTGGCCACTGGGCACTGTCTCAA 2040
 GAAGTCAGGATCACACACTCAGTCTTGTGTTCTCTCCAGGT 2080
 CCTTGTCTCTGTCTCTGGGGAGGGAGGCAAGAGTGTCTG 2120
 TCTGTCTCTCTCTCTCTGTCTGTCTGTCTGTCTCTCTCT 2160
 CATCTGTCTCTCTCTCTCTGTCTGTCTGTCTGTCTCTCT 2200
 ACAGTGTGGCTCAGGGGCAATAAACTCTGCTCTGACTCC 2240
 TCTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2280
 AAAAAAAAAAAAAAAAAAAAAA 2301

Figure 10B

mmFATP4 protein sequence

HASAHASGMALGVFAALININLRRDALRHCLDTSKARAL 40
 IFGSEMASAICETHASLEPTILSLFCSGSWEEPSTVFVSTEH 80
 LDPLLEDAPKHLPSHPDKGFTDKLFYIYTSGTIGLEPKAAT 120
 VVHSRYRMASLVYYGFRMRPDDIVYDCLEPLYHSSFRKRG 160
 DWQCLIHGMLVIRKKFSASRFWDDCIKYACTVVOYIGEL 200
 CFYLLNQPPREAESRHKVRMALGNGLRQSIWIDFSSRFHI 240
 PQVAEFYGATECNCSLGNFDSRVGACGENSRILSFVYPIR 280
 LVRVNEDIMELIRGPDGVCTPCQPGQPGQLVGRITIQODPL 320
 RRFDDGYLNQGANMKLIANDVFKKGDQAYLITGVLMDELG 360
 YLYFRDRIGDIFRWKGENVSTIEVEGHLSRLIHMAWAVY 400
 GVEVPGTIEGRAGMAAVASPLSNCDLESFAQILKKELPLYA 440
 RPIFLRFLPELHKIGTFKFKQKTELKKEGFDPSVWKDPLFY 480
 LDARKGCVVALDQFAYIRIQAGEEKL 507

Figure 11

mmFATP5 DNA sequence

CACATCATCAGAGCTAAGAGAGACTACACGCTCTCATCTAC 40
 TTCAGAAAGAGCCAAATGOCATGGGATTTTGAAGAAACTA 80
 ACCTTACIGCTGTGTGCTGCTTCTGCTGGGTGGGCTGGGGC 120
 AGCCCCCATGGCCAGCAGCTATGGCTCTGGGCTGGGTG 160
 GTTCCCTGGGAGACCCACATGCTGTGTGCTGTGGCTGTG 200
 GCATTGCTGGGCGAGACCGTGGATCAGCTCCCTGGATGCCCC 240
 ACCTGGCTGAGCCCTGGTAGGAGCAGCTCTTACCTTATTCCT 280
 ATTGCTCTCTACAGCCACCCCGAGGGCTACGGCTGGCTGCAT 320
 AAAGATGTGGCTTTTACCTTCAAGATGCTTTTCTATGGCC 360
 TAAAGTTTACGGCGACCGCTTAAACAAACATCCTCCAGAGAC 400
 CTTTGTGGATGCTTTAGAGCGGCAAGCAGCTGGCATGGCT 440
 GACCGGGTGGGCTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 480
 CAATCACAATAAGCCAGCTGGATGCCAGGTCCTGTGTGTGT 520
 AGCATGGGTCTGTAAAGCAAAGCTGAAGGATGCCGTATATC 560
 CACAACACAAGAGATGCTGTGTGTGTGTGTGTGTGTGTGTGT 600
 CCAAGACCATTTTCTGTGTGTGTGTGTGTGTGTGTGTGTGT 640
 CAAGTTGGGCTGGGCTGTGTGTGTGTGTGTGTGTGTGTGTGT 680
 CGAGGATGGGCTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 720
 CCAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT 760
 GGAAGAAGTCTCTTCCCAAGCTGTGTGTGTGTGTGTGTGTGT 800

Figure 12A

662250-40550460

094055040550460

TGCTTCTACCTTGGGCTACAGCTCAACCAACCCGGGAGTAG 840
AGGCTCTGGGAGCTTCCCTGCTATGCTGCACTTCTGACCC 880
AGTACCTGGGAGCTTCCGAGCTACGATTAAAGTGGAAATCT 920
CCGCGCATATTCATCTTTACTTTCAGGGACCACTGGTACTCC 960
CAAAGCCAGCATCTTTATACATGAGCGGCTCATAACAAGT 1000
GAGCAACCTGCTGTGCTTCTGTGGATGCAAGAGCTGATCAT 1040
GTTGCTATGACGTCCTTACCTCTGTACCATACGATAGGGC 1080
TTGTCCCTTGGATTCCCTTGGCTGCTTACAAGTTCGAGCCAC 1120
CTGTGTCTCTGGCCCCCAAGTTCTCTGCTTCCCGATTCTGG 1160
GCTGAGTGGCCCGCAGCATGGCGTAAACAGTCACTCTGTATG 1200
TGGCTGCAAAATCCCTGCGGTACTTGTGTAAAGTCCCTGAGCA 1240
ACCAGAAGACAAGATACATACAGTGGCGCTTGGCCATGGGA 1280
ACTGGACTTCCGGGCAAAATGTGTGGA AAAACTTCCAGCAAC 1320
GCTTTGGTCCCATTTCCGATCTGCGAATTCTACGGATCCAC 1360
AGAGGGCAATGTGGGCTTAAATGAACATGTGGGCGCACTGC 1400
GGGGCTGTGGGAAGCAACAGCTGCATCCCTTGGAAATGCTGA 1440
CTCCCTTTGAGCTTGTACAGTTCCACATAGAGACAGCAGA 1480
GCTCTGAGGGACAAACAGGGTTTTTTCATTCTGTGGAG 1520
CCAGGAAAGCCAGGACTTCTTTTGAACCAAGGTTGAAAGA 1560
ACCAACCCCTTCCCTGGGCTACCGTGGTTCCAGGCGGAGTC 1600
CAATCGGAAACTTGTGTGGGAATGTACGACCGGTAGGAGAC 1640
CTGTACTTCAACACTGGGGACGTGCTGACCTTGGACCCAGG 1680
AAGGCTTCTTTTACTTTCAGAACCGGCTTGGTACACCTT 1720
CCGGTGGCAAGGCGGAAAACGTATCTACTGGAGAGGTTGG 1760
TGTTGTTTTGTCTAGGCTAGACTTCTAGAGGAAGTCAATG 1800
TCTATGGTGTGCTGTGCTGAGGCTGAGGGTAAAGGTTGG 1840
CATGGCTGCTGTGAAACTGGCTTCTGGAAGACCTTTTTCAT 1880
GGGCAGAAAGCTATACAGCATGTGCGGCTCTGCGCTCCCTG 1920
CCATATGGCCACACCTCATTTTCATCCGTATCCAGCATTCCT 1960
GGAGATCACAACACCTTACAAGCTGGTAAAGTCAAGGCTG 2000
GTGGGTGAGGGTTTTGATGTGGGATCATTTGCTGACCCCC 2040
TCTACATACTGGACAACAAGGCGGACACCTTCCGGAGTCT 2080
GATGCCAGATGTGTACAGGCTGTGTGTGAAGGAACCTGG 2120
AATCTCTGACCACCTAGCCAACTGGAAGGCAATCCAAAAG 2160
TGTAGAGATTGACACTAGTACAGCTTCAAAAGTTGTCCGG 2200
GTTCAGATGCCCCATGGGCCAGTACTTACATAGACAATAAA 2240
CTTGAATGTGTATACAAAAA AAAAAAAAAAAAAAAAAA 2277

Figure 12B

mmFATP5 protein sequence

MALALRWFLGDPTCLMLIGLALLGRFWISSWMEHWSLVG 40
 AALITLFLPLQPPRGLRWLHKDVAFIFKMLFYGLKFRRL 80
 NKHPPEIFVDALERQALAWPDRVALVCTGSEGSSTINSOL 120
 DARSQAAWLWKLKDAVIONIRDAAAILMLPSKTTISAL 160
 SVFLGLAKLGCPVAVINPHSRGMPLIHSVRSSGASVLIVD 200
 PDLQENLEEVLPKLLAENIHCFYLGHSSPTGVEALGASL 240
 DAAPSDFVPASLRATTKWKSPAIFIFTSGITIGLEPKPAIL 280
 HERVIQVSNVLSFCGRADDVVDVLPYHTTIGLVLGFLG 320
 CLQVGCATCVLAPKFSASRFWAECRQHGVTIVILYVGEILRY 360
 LQWPEQPEDKLIHIVRLAMGTGLRANVWKNFQRFGPTRI 400
 WEFYGSIEGNVGLMNYVGHGAVGRTSCILMLIPPELWQ 440
 EDIEIAEPLRDKQGFCLFVEFGKPGILLIKVRKNQPFILGY 480
 RGSQAESNRKLVANVRRVGDLYFNIGLMLILDQEGFFYFQ 520
 DRLGDIFRWKGENVSTIGEVECVLSSLDLEEVDVYGVFVP 560
 GCEGKVGMAAVKLAPEKTFDQKLYQHVRSLPAYATEHF 600
 IRIQDSLETINTYKLVKSRLVREGFDVGLIADPLYILINK 640
 AQIFRSLMPDVYQAVCEGIWNL 663

Figure 13

hsFATP2 DNA sequence

ATGGGATTGACTCTTTTCTGACAAAGTGCATGAAGTATC 40
 AACTGAACCTATCCCAGAGTCATGCAGGCTGAAGTACT 80
 TTTTCCACTCCTGCGTTATACATTTATACITTCIGCAACCA 120
 CAGGCTTCCAAAAGCAGCCATGATCACTCATCAGCGCAT 160
 ATGGTATGGAACCTGGGCTCAGTTTGTAGCGGATTGAAG 200
 GCAGATCATGTCATCTATATCAGTCTGCGGCTTTTACCACA 240
 GTCCTGCACTACTGATTGGCATTACCGATGTATTGIGGC 280
 TGGTGGTACTCTTGGCTTGGGACTAAATTTTCAGCCAGC 320
 CAGTTTGGGATGACTGCAGAAAATACAACGTCACTGTCA 360
 TTCAGTATATCGGTCAGTCTGCTTGGTATTTATGCAACTC 400
 ACCACAGAAACCAATGACCGGATCATATAAGTGAGACTG 440
 GCACTGGGAAATGGCTTACGAGGAGATGIGGCGACACAAT 480
 TTGTCAAGAGATTTGGGGACATATGCATCTATCAGTTCTA 520
 TGCCTGCCACTGAGGCAATATTGCAATTTATGAATTATCG 560
 AGAAAAGTTGGGCTGTTGGAAGAGTAAACTACCTACAGA 600
 AAAAAATCATAACTTATGACCTGATTAAATATGATGIGGA 640
 GAAAGATGAACCTGTCCGTCATGAAAATGCATATTGGGTC 680
 ACAGTTCGCCAAAGGTGAAGTTGCACTTCTGGTTTGCAAAA 720
 TCACACAACCTACACCATTTAATGGCTATGCTGGAGCAA 760
 GGCTCAGACAGACAAGAAAAACTGACAGATGCTTTAAG 800

Figure 14A

AAAGGAGACCTCTATTTCACAGTGGAGATCTCTTAATGG 840
 TTCAACCATGAAAATTTTCATCTATTTCACGACAGAGITGG 880
 AGATACATTCCGGTGGAAAGGGGAAAATGTGGCCACCCT 920
 GAAGTTCCTCATATAGTTCGACCTGGTTGATTTTTTCCAA 960
 CGAAGTAAAATGTTTATGGGAGTGCATGGGCCAAGATNAT 1000
 CGAGGTTTCGAATTTGGCATGGCNITCCNITCAAATGGAAA 1040
 GAAAACCATGCAATTTGATGCAAAGCAATTTTTTTCAGNAC 1080
 ATTGCTGATAACCNACCTAGTTATGCAAGGCCCCGGTTTT 1120
 NTAAGANACAGGACACCATTTGAGATCAGTGAATTTTTA 1160
 AACACCGCAAAATGAOCTTTGGTGGAGGAGGGCTTTAACC 1200
 CNGCTGTCATCAAAGATGCCCTTGTATTTTCTTGCATGACA 1240
 CAGCAAAAATGTATGTGCTATGACTGAGGACATNATAA 1280
 TGCCATAAGTGNIAAAAACCTGAAATINIGAAATATTCOCA 1320
 GGAGGATAATTCAACATTTCCAGAAAGCAAACTGAATGCAC 1360
 AGCCACTTGATATAATCCAACCTTTAATTTGATTTGAAGATT 1400
 GTGAGCAAATTTTGTAGCAAATTTGCATACCCGTAAAGGG 1440
 AGACTTTTTTAAATAACAGTTGAGTCTTTGCAAGTAAAAA 1480
 GATTTAGAGATTATTATTTTTTCAGTGTGCACCTACIGTTT 1520
 GTATTTGCAAACCTGAGCTTGTGTGGAGGGAAGGCATTATTT 1560
 TTTAAAATACTTAGTAAATTAAAGAACACCAACATGTIGAA 1600
 AAAAAAAAAAAAAAAAAAAAAA 1622

Figure 14B

hsFATP2 protein sequence

YIYISGTTGLPKAAMTHQRIWYGTGLTFVSGLKADDVIY 40
 ITLPPFYHSAALLIGHGCI VAGATLALRIKFSASQFWDDC 80
 RKYNMIVIQYIGELLRYLQNSPQKENDRDHKVRLALGNEL 120
 RGDWRQFVKRFGDICTIYEFYAATEGNIGEMNYARKVGAV 160
 GRVNYLQKKILTYDLIKYEVEKDEFVRDENGVCVRVEKGE 200
 VGLLVCKTITQITPFNGYAGAKAQTEKKLRDVFKKGLDYF 240
 NSGDLIMVDHENFTYFHDRVGDITFRWKGENVATTEVADIV 280
 GLVDF 286

Figure 15

hsFATP3 DNA sequence

CAATTGGGGACCCCCAGGGGCACTGTATGGCCACATCTCC 40
 AGGTGAGCCAGGGGAAGTTGCTAAAGCATGTCTTCGGGCC 80
 TGGGGATGTTTTCTTCAACACTGGGGACCTGCTGGTCTGC 120
 CATGACCAAGGTTTTCTCCGCTTCATGATGGTACTGGAG 160

Figure 16A

ACACCTTCAGGTGCAAGGCGAGCAATGTGGCCACAACCGA 200
 GGTTGCCAGAGGTCTTTCAGGCGCTAGATTTTCTTCAGGAG 240
 GTCAAGGTCTATGGAGTACAGTGTGGCCAGGGCATGAAGGCA 280
 GGGCTGGAATGGCAGCCCTAGTTCTGGTCCCCCCCCAAGC 320
 TTTGGACCTTATGCAGCTCTACACCCAGTGTCTGAGAAC 360
 TTGCCACCTTATGCCCCGGCCCCGATTTCCTCAGGCTCCAGG 400
 AGTCTTTTGGCCACCACAGAGACCTTCAAAACAGCAGAAAGT 440
 TCCGATGGCAAAATGAGGGCTTTCAGCCCCAGCACCCCTGTCT 480
 GACCCACTGTACGTTCTGGACCCAGGCTGTAGGTGCCCTACC 520
 TGCCCCCTCACAACCTGCCCCGGTACAGCGCCCTCCTGGCCAGG 560
 AAACCTTCGAATCTGAGAACTTCCACACCTGAGGCACTTG 600
 ACACAGCAACTCTGTGGGGGGGGGGGGGGGGGGGGGGGGGG 640
 TGGGCTGTACAGGCACTTTTCTATACCACTGCGGTCA 680
 CTATTTTGTAAATAAATGTGGCTGGAGCTGATCCAGCTGTC 720
 TCTGACCTACAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 753

Figure 16B

hsFATP3 protein sequence

QFGTFRGIVWPHLQVSQKLLKIDVERPGDVFFNIGDLIVC 40
 DDQGFLEFHDRTIGDIFRWKGENVATIEVAEVFEALDFLQE 80
 VNVYGVIVFGHEGRAGMAALMLRPPHALDIMOLYTHVSEN 120
 LPPYARPRFLRLQESLATTEIFKQOKVRMANEGFDPSTLS 160
 DPLYVLDQAVGAYLPLTTARYSALLAGNLR 191

Figure 17

hsFATP4 DNA sequence

TCAAGTACAACCTGCACGATTGTTCATANCATTGGTGAACCTG 40
 TGGCGNTACCTCCTGAACACAGCCACCGCGGGAGGCAGAAA 80
 ACCAGCACCCAGGTTCCGATGGCAGTACGCAATGGCCCTCCG 120
 GCAGTCCATCTGGACCAACTTTTCCAGCCGCTTCCACATA 160
 CCCCAGGTGGCTGAGTTTATAGGGGGCCACAGAGTGCAACT 200
 GTAGCCTGGGCAACTTCGACAGCCAGGTGGGGGCTGTGG 240
 TTTCAATAGCCGCATCCTGTCTTCTGTGTACCCCATCCGG 280
 TTGGTACGTTGTCAACGAGGACACCATGGAGCTGATCCGGG 320
 GGGCGGAGGGGCTGTGCTTCCCTGGCAGCCAGGTGAGCC 360
 GGGCCAGCTGGTGGGCGCATCATCCAGAAAGACCCCTG 400
 CGCCGCTTCGATGGCTACCTCAACCAGGGCGGCAACAACA 440
 AGAAGATTGCCAAGCATGTCTTCAAGCAAGCGGGACAGGC 480
 CTACCTTACTGGTGATGTCTGTGTATGCACGAGCTGGCC 520

Figure 18A

09405504-092399

TACCTGTACTTCCGAGACCGCACTGGGGACACGTTCCGCT 560
 GCAAAGGTGAGAAAGGTGTCCACCAACGAGGTGGAAGGCAC 600
 ACTCAGCGCGCTGCTGGACATGGCTGACGTGGCGGTGTAT 640
 GGTGTCCAGGTGCCAGGAACCGAGGGCGGGCGCGGAATGG 680
 CTGTCTGTGGCCAGCCCCACTGGCAACTGTGACCTGGGAGC 720
 GCTTTGCTCAGGTC 734

Figure 18B

hsFATP4 protein sequence

IGELCRYLLNQPPREAFNQHVRLALGNGLRQSIWINFSS 40
 RFHIPQVAEFYCAETHCNSLGNFDSQVACCFNSRILSFV 80
 YPIRLVRVNEUIMELIRGPDGVCIPQGFEGQLVGRILQ 120
 KDPLRRFDGYLNGANNKKIAKLVFKKGDAYLITGDLVM 160
 DELGYLYFRDRITGDIFFWKGENVSTTEVEGILSRLLIMAD 200
 VAVYGVVEVFGIEG 213

Figure 19

hsFATP5 DNA sequence

CNIGCCTLTGTACCAAGGATGGGACTTTGTGCTTGGGA 40
 TCCTCGGCTGCTTAGATCTGGAGCCACCTGTGTCTGGC 80
 CCCCAGTTCTCTACTTCCCTGCTTCTGGGATGACTGTGG 120
 CAGCATGGCGTGACAGTGATCTCTGTATGTGGGGGAGCTCC 160
 TGGCTTACTTGTGTATACATTCCCCAGCAACCAAGGACCG 200
 GACACATACAGTCCGCTGGCAATGGGCAATGCACTACCG 240
 GCTCATGTGTGGCGGACCTTCCAGCAGCGTTTGGGTCCT 280
 ATTTCGGATCTNGGGAAGTCTTACGGGCTYCCACAGAGG 320
 GCAACATGGGGCTTTAGTTCAACTATTGTTGGGGGGCGCTG 360
 CGGGGSCCTNGRGGCAAGATGGAGCCTGCTCTCTCCGAA 400
 TGCTGTCCCCCTTTGAGCTGGTGCAGTTGCATGCGAGGC 440
 GGCGGAGCCTGTGAGGGACAATCAGGGCTTCTGCACTCCCT 480
 GTAGGGCTAGGGGAGCGGGGCTGCTGTGACCAAGGTTG 520
 TAAGCCAGCAACCCCTTGTGGGCTACCGGGCCCCCGAGA 560
 GCTGTCCGAACCGAAGCTGGTGGCAACGTTGGGCAATCG 600
 GGCGACGTTTACTACAAACACCGGGGACGTAAGTGGCCATGG 640
 ACGGCAAGGCTTCTCTACTTCCGCAACGACTGGGGCA 680
 CACCTTCCGATGCAAGGGCGAGAAGGTGTCCACGCAAGAG 720
 GTGCAAGGGCGTGTGTGTGCGAGGTGGACTTCTTGCAACAGG 760
 TTAAGGTGTATGGCGTGTGGTGGCAGGTTGTGAGGGTAA 800
 GGTGGGCATGGCTGCTGTGGCATTAGCCCCCGGGCAGCT 840

Figure 20A

TTGGACGGGGACAAGTTGTACCAGCAAGTTGGGGCTTGGC 880
 TCCCTGGCTAAGCTACCCCCCATTTTCATCCGCATCCAGCA 920
 CGCCATGGAGGTCACACAGCAGTTCAAACCTGATGAAGACC 960
 CGGTTGGTGGGTGAGGGCTTCAATGTGGGGATCGTGGTTG 1000
 ACCCTCTGTTTGTACTGGACAACCGGGGGCCAGTCCCTCCG 1040
 GCCCCTGACGGCAGAAATGTACAGGCTGTGTGTGAGGGA 1080
 ACCTGGAGGCTCTGATCACCTGGGCAACCCACGGGGTAG 1120
 GGATCAAAGCCAGCCACCCCAACCCACACACTCGGTGT 1160
 CCGTTTCATCCCTGGGCTGTGTGAATCCAGCCCTGGCCAT 1200
 AOCCTCAACCTCAGTGGGCTGTAATGACAGTGGGCCCCG 1240
 TAGCAGTGGCAGAAATAAACTCAGTGTGTTCACAGAAA 1278

Figure 20B

hsFATP5 protein sequence

EGQHGALVQLLLGALRGFGKDGACLLRMLSPFELVQFLM 40
 EAAEFVRINQGFCLPVGLGEPGLLLTKVWSQOPFVGYPGP 80
 RELSERKLVNRVRSGLVYNTIGDLAMDREGFLYFRDL 120
 GDTFRWKGENVSTHEVEGLSQVDFLQQNVYGVCPGCE 160
 GKVGMAAVALAPGQTFDGEKLYQHVRWLPAAYATPHFIR 199

Figure 21

hsFATP6 DNA sequence

CGCTTGTGTGTTAAAGAAGAAATTTTCAGCAAGCCAGTTT 40
 TGGAGTGACTGCAAGAAGTATGATGTGACTGTGTGTTTCA 80
 ATATTGGAGAACCTTGTGGCTACCTTTGCAACAATCTAA 120
 GACAGAGCAAGAAAGCATCATAAGGTGGGTTTGGCAATT 160
 GGAAATGGCATAACGAGTGATGTATGCAGAGAAATTTTAG 200
 ACAGATTTGGAAATATAAAGGTGTGTGAACCTTTATGCAGC 240
 TACCGAATCAAGCATATCTTTTCATGAACCTACACTGGGAGA 280
 ATTGGAGCAATTGGGAGACAAATTTGTTTTACAACTTC 320
 TTTCACCTTTTGACTTAATAAAGTATCACTTTTCAAGAGA 360
 TGAACCCATGAGAAATGAGCAGGGTTGGGTATTCATGAGA 400
 AAAAGCAGACCTGGACTTCTCATTTCTCGAGTGAATGCAA 440
 AAAATCCCTTCTTTGGCTATGCTGGGGCTTATAAGCACAC 480
 AAAAGACAAATTGTCTTGTGATGTTTTTAAGAGGGGAGAT 520
 GTTACCTTAATACCTGGAGACTTAATAGTCCAGGATCAGG 560
 ACAATTTCCCTTATTTTGGGACCGTACCTGGAGACACTTT 600
 CAGATGCAAGGAGAAATGTGGCAACCACTGAGGTGCT 640
 GATGTATGTGAATGTGTGATTTTCATACAGGAAGCAAG 680
 TCTATGGTGTGGCTATATCAGGTATGAAGCAAGAGCAGG 720

Figure 22A

Figure 22B

Figure 23

Figure 23

Figure 24A

Figure 24A

TTCGGCGGCGGGGGCTGGCGCCCGGCCAAGTTCGTTCGCA 400
TCATGTTGGTAACTCACCACGCACAGTCTTGCGCATGCT 440
GGCCACGGGTCAGTGGGGCGCTATTGGCGGCATGCTCAAC 480
TAACACAGCGGGGAGGTGTGGCGCACAGCGCTGGGTIC 520
TGCTGGACGGCAAGGTACTGATCGCACAGTCCGACTTGGT 560
CAGCGCGGTTCGCGAATGCGCGCGCTTGGCGGGCGGGGA 600
GGGGGCGACGTGCTGAACCGTTCAGGACGTGGAGCGATTGG 640
CCACAACGGCGCGCGGCAACCAACCGCGGTTCGGGTTCGGC 680
CGTGCAAGCCAAGACACCGCGTTCTACATCTTCACCTTCG 720
GGCACCAACGGGATTTCCCAAGGOCAGTGTTCATGAAGCATC 760
ATCGGTGGCTGGGGCGCTGGCGGTCTTTCGACGGCATGGG 800
GCTGGGGCTGAAGCGTTCCGACAGGCTCTACAGCTGCGTG 840
CGCGTGTACCAACAACCGGTAAACGGTTCGGGTGTCTGT 880
CGGTGATCAATTCTGGGGCGAACCTTGGCGCTGGGTAGTIC 920
GTTTTTCGGGTTCGGGTCTTGGCATGAGGTGATTGGCAAC 960
CGGGCGACGGGTTCGTCTACATCGCGCAAATCTGCGGT 1000
ATCTGCTCAACACAGCGCGGCAAGCGACCGACCGTTCGCA 1040
CCAGGTGGGGTTCATCTCGCGTAACGGGCTGGCGCGGGAG 1080
ATCTGGGATGAGTTCACCAACCGCTTCGGGCTCGCGCGGG 1120
TGTCGAGTCTACCGCGCCAGCGAAGGCAACTCGCGCTT 1160
TATCAACATCTTCAACGTGGCCAGGACCGCGGGGTATCG 1200
CCGATGCGCGCTTGGCTTTGTGGAAATACGACCTGCACACG 1240
GOGATCGCGTGGGATGCGAGCGGGCGAGTGGGTTCGGT 1280
ACCGCACGGGTCAACCGGGCGCTGTTGCTTAGCGGGTCAAC 1320
CGGCTGCAGCGGTTCGACGGCTACACCGACCGCGGTTCGA 1360
GCGAAAAGAAGTTCGGTGGGCAACGCTTTTCGAGATGGGA 1400
CTGTTCGGTCAACAACCGGTGACGTGATGAGCGCGTAGGGC 1440
ATGGGCGATCGCGCGCTTCGTTCATCGGCTGGGCGACACCT 1480
TCCGCTGGAAGGCGGAGATGTGGCAACCACTCAGGTTCGA 1520
AGCGGCACTGGCTTCGACCGACACCGTTCAGGAGTTCAG 1560
GTCTACCGGCTCCAGATTCCGGCGACCGGGGGGGGGCGG 1600
GAATGGCGCGCATCACACTCGCGGCTGGCGCGCAATTTCGA 1640
CGGCGAGGCGCTGGCGCGAACGGTTTACGGTCACTTGGCC 1680
GGCTATGCACTTCGGCTCTTTGTTCGGGTAGTGGGGTGGC 1720
TGGCGCACACAGGAGTTCACAGTCCAGGTGGAGIT 1760
GCGCAACAGGCGCTATGGCGCGGACATCGAGCATCCGCTG 1800
TAGCTACTGGCGCGCGCGCAACGAAGCATATGTGCGGTACT 1840
ACGCGCAATAACCTCAGGAGGTTTCGCTCGCAAGGCGACC 1880
GCAGGGCTAGCGGATTCGGCGCGAGTCTCGATAACCGCA 1920
CTGCAACGCTCGACGGTAACAGGCACTATGGATCGGTGG 1960
TTCAACACCGCGCGGCTCAGCGGCTCGTTCACACACCGCG 2000

GGGTAG 2007

Figure 24B

mtFATP protein sequence

msdyggahttvrlidlatmprvladtgvivrgamtgll 40
anpnskasigtvfgdraarygdrvflkfgdqiltyrana 80
tanryaavlaargvgpgdvvgimlmspstvlamlatvkc 120
gaiagmlnyhgrgevlahslglldakvliaesdlvsavae 160
ogasgrvagdvltvedverfattapatnpasasavqakd 200
tafyiftsgttgfpkaswmthhrwlravfggnglrllkg 240
sdtlyscplplyhnmaltvavssvinsgatllalgksfsasr 280
fwdevianratafvyigeicryllngpakptdrahqvrvi 320
cgnglrpeiwdettrfgvarvcefyasegnsafinifn 360
vprtagvspmplafveydlldtgdlrdasgrvrrvpdgep 400
glllsrvnrlopfdytdpvasekklvmafrdgdowfnt 440
gdvmspgmgghaafvdrldgtfrwkgenvattqveaalas 480
dgtveectvygvqiprtggragmaaitlragaefdgqala 520
rtvyghlpgyalplfvrvvgslahtttfksrkvelmqay 560
gadiedplyvlagpdgyvpyyaeypeevslgmpgg 597

Figure 25

65260:10550160

66260"4050460

hsFATP1

1 tgc acc cag ggc gtc cgg gac ccc aaa gca gaa gcc cgc aca gta ggc aca ggc cag cca
61 aga agg gtc cag gag tct gca gaa aca gaa agg tcc ccg gcc tca gcc tcc tag tcc ctc
121 cct gcc tcc tgc ctc agc ttc tgg gag act gaa ggc acg gct tgc agc ttc agg act cgg
M R
181 gct ccg ggt ggc ggc ggc gcc tgc gtc tgc ctc ggc ctc tgc tgc ggc ctc
A P G A G A A S V V S L A L L W L L G L
241 ccg tgg acc tgg agc ggc gca ggc cgc ctc ggc gtc tac gtc ggc agc ggc ggc tgc cgc
P W T W S A A A A L G V Y V G S G G W R
301 ttc ctc cgc atc gtc tgc aag acc ggc agc cga gac ctc ttc ggt ctc tct gtc ctc atc
F L R I V C K T A R R D L F G L S V L I
361 cgc gtc cgc tgc ggc ggc ggc gcc cgc cgc cgc cgc cgc cgc cgc cgc cgc cgc cgc
R V R L E L R R H Q R A G H T I P R I F
421 cag ggc gta gtc cag cga cag ccc gag cgc ctc ggc ctc gtc gat gcc ggc acc ggc gag
Q A V V Q R Q P E R L A L V D A G T G E
481 tgc tgg acc ttc ggc cag ctc gac gcc tac tcc aat ggc gta gcc aac ctc ttc cgc cgc
C W T F A Q Q L D A Y S N A V A N L F R Q
541 cgc ggc ttc ggc cgc ggc ggc ggc ggc ggc ggc ggc ggc ggc ggc ggc ggc ggc ggc
L G F A P G D V V A I F L E G R P E F V
601 ggc ctc tgc ggc ctc ggc gcc agc ggc agc ggc ggc ggc ggc ggc ggc ggc ggc ggc ggc
G L W L G L A K A G M E A A L L N V N L
661 cgc cgc gag ccc ctc ggc ttc tgc ctc ggc gcc acc cgc ggc gct aag gcc ctc acc ttc gga
R R E P L A F C L G T S G A K A L I F G
721 gga gaa atg gtc ggc ggc ggc gcc gaa gtc agc ggc cat ctc ggc aag agt ttc acc aag
G E M V A A V A E V S G H L G K S L I K
781 ttc tgc ttc gga gac tgc ggc ccc gag ggc atc ttc cgc gac acc cag ctc ctc gac cgc
F C S G D L G P E G I L P D T H L L D P
841 ctc ctc aag gag gcc tct acc gcc ccc ttc gca cag atc ccc agc aag ggc atg gac gat
L L K E A S T A P L A Q I P S K G M D D
901 cgt ctt ttc tac atc tac acg tgc ggc acc acc ggc ctc ccc aag gct gcc att gcc gtc
R L F Y I Y T S G T T G L P K A A I V V
961 cag agc agg tac cgc atc gca gcc ttc ggc cag cag gcc tac cgc atg cag ggc ggc
H S R Y Y R M A A F G H H A Y R M Q A A
1021 gac gtc ctc tac gac tgc ctc ccc ctc tac cag cgc gga aac atc atc ggc gtc ggc
D V L Y D C L P L Y H S A G N I I G V G
1081 cag tgc ctc atc tac ggc ctc aca gtc gtc ctc cgc aag aaa ttc tgc gcc agc cgc ttc
Q C L I Y G L T V V L R K K F S A S R F
1141 tgc gac gac tgc atc aag tac aac tgc acg gtc gtt cag tac atc ggc gag atc tgc cgc
W D D C I K Y N C T V V Q Y I G E I C R
1201 tac ctc ctc aag cag cgc gtc ggc gag cgc gag agc cga cgc ctc gtc ctc ggc gtc
Y L L K Q P V R E A E R R H R V R L A V
1261 ggc aac ggc ctc gtc ctc gcc atc tgc gag gag ttc acg gag cgc ttc ggc gta cgc caa
G N G L R P A I W E E F T E R F G V R Q
1321 atc ggc gag ttc tac ggc gcc acc gag tgc aac cgc agc att gcc aac atg gac ggc aag
I G E F Y G A T E C N C S I A N H D G K
1381 gtc ggc ttc tgc gtc ttc aac agc cgc atc ctc ccc cag gtc tac ccc atc cgc ctc gtc
V G S C G F N S R I L P H V Y P I R L V
1441 aag gtc aat gag gac aca atg gag ctc ctc cgc gat gcc cag ggc ctc tgc atc ccc tgc
K V H E D T M E L L R D A Q G L C I P C
1501 cag gcc ggc gag ctc ggc ctc ctc gtc ggc cag atc aac caa cag gac cgc ctc cgc cgc
Q A G E F G L L V G Q I N Q Q D P L R R
1561 ttc gat gcc tat gtc agc gag agc gcc acc agc aag aag atc gcc cag agc ttc ttc agc
F D G Y V S E S A T S K K I A H S V F S
1621 aag ggc agc ggc gcc tac ctc tca ggc gac gtc cta gtc atg gat gag ctc ggc tac atc
K G D S A Y L S G D V L V M D E L G Y M
1681 tac ttc cgc gag cgc agc ggc ggc gcc acc ttc cgc tgc cga ggc gag aac gtc tcc acc acc
Y F R D R S G D T F R W R G E N V S T T
1741 gag gtc gag ggc gtc ctc agc cgc ctc ctc ggc cag aca gac gtc gcc gtc tac ggc gtc
E V E G V L S R L L G Q T D V A V Y G V
1801 gct gtc cca gga gtc gag ggc aag gca ggc atg ggc gcc gtc gca gac ccc cag agc ctc
A V P G V E G K A G H A A V A D F H S L
1861 ctc gac ccc aag cgc ata tac cag gag ctc cag aag gtc ctc gca ccc tat gcc cgc ccc
L D P N A I Y Q E L Q K V L A P Y A R P
1921 atc ttc ctc cgc ctc ctc ccc cag gtc gac acc aca ggc acc ttc aag atc cag aag acg
I F L R L L P Q V D T T G T F K I Q K T
1981 agc ctc cag cga gag ggc ttc gac cca cgc cag acc tca gac cgc ctc ttc ttc ctc gac
R L Q R E G F D P R Q T S D R L F F L D
2041 ctc aag cag ggc cag tac ctc ccc tta aat gag gca gtc tac act cgc atc tgc tgc ggc
L K Q G H Y L P L N E A V Y T R I C S G
2101 gcc ttc gcc ctc tga agc tgc tcc cct acc ggc cag aaa ctc tgc gcc tgc tgc gag agc
A F A L *
2161 cca gct tga gcc aga cag cgc tgc cca ggc gtc gcc gcc tag tac aca ccc acc tgc cgc
2221 agc tgc acc tgc cag gcc cca tcc tgc act gag aaa ctc gaa cct cag agc aac cgc tgc
2281 ctc tct gct gcc tgc gtc ccc ctc gtc ctc cct ctc cct gct ttc cag cct ctc ttc
2341 cct tcc atc cct gtc cct gtc tgc ccc taa ctc ttc cct ctc ttc ttc ttc cct ttc
2401 ttc ttc ttc ttc aag ata gag tct cag tct gct gcc cgc gct aga gtc cag tgc tgc gat
2461 ctc ggc tca ctc caa cct ctc cct ccc ggc gtc caa gtc atc ctc cca cct cag cct cct
2521 gag tag ctc gga tta cag gca ccc gcc acc acc tcc agc taa ttt tta tat ttt tag tag
2581 aga cgc ggc ttc acc atg tgc gtc agc ctc gtc tgc aac tcc tga cct cag gtc atc cgc
2641 tgc cct cgc cct ccc aga gtc ctc gga tta tag ggc tga gcc tct ggc cgc gcc ttc cct
2701 ttt tcc tct cct ctc ctc cgc aga gtc gaa cag agc tgc cct ggc agc tgc atc ttc tgc
2761 agc gtc cag ctc ttc tgc ggc act gca gga atc atc ccc cct ggc ccc tgc act cgc act
2821 ggc gcc tcc cca cct ccc cgc cgc ctc gtc ctt acg gag ccc caa tcc agc cct cct gtc
2881 gct gct ggc ttc cag atg ctc cag ccc cat gtc act tcc aag cag gcc ctc cgc cct ccc
2941 tgc tga atg gag gag cgc ggc gtc ccc cag gcc aac tgc aaa atc tcc cag gct agc cca
3001 act gcc ttt tgc act tcc cgc ttc ctc tca cat ttc ccc agc ccc acc ttc ccc tcc tga
3061 tgc cct gaa agc ttc cgc aat tga ctc tga cca ctt gga tgc cag cag tgc cag ccc ctc
3121 cct tga tgc ccc cag tta gcc atc tcc atg gag ctc ctc ctc gag ggc cct gaa ccc tgc
3181 act ggc tgc ctc ccc agc cag ctc cct cct gtc ctc gga gga ggc ctc ctc ggc gtc ctc
3241 atc tgc tgc gtc cag tgc agc gtc cca cag gag agc cag cag agc ggc cag ggc agc tct
3301 cct gcc ggc ggc tgc cct ctc aag cct cag ggc ttc tag cct gct gaa tat acc cca cct
3361 ggc ggc tgc ccc ctc cga tgc ccc cag tga tgc ctc tga cag cgc gct ggc ggc gat gtc
3421 cca gac aac ccc acc agc agc gcc cag aca tcc cta ctc gct cgc ctc gtc gct cat ctc
3481 gaa cat cca cgc cag cct ttc tgc ggc cgc cca ccc agc cgc cct gtc cgc ctc tcc tcc
3541 ctc cag cag ccc ctc gcc cct gga gtc gtc ggc cca tgc caa gag aca cgc tgc cgt
3601 ctc atg tga acc ttc ctc ggc act gtc gtc tta ttc cct aat tga ttc aag aaa taa acc
3661 tga aga cgc tcc ggt gaa aaa aaa aaa aaa agc ggc gcc gc

hsFATP4

```

1    cga ccc acg cgt ccg ggc ggg cgg ggc cgg gcg gcg ggc ggg gct ggc ggg gcg gcc ggg
61   cca tgc agg gcg cag agc cgg cta aac cct gct gag acc cgg ctc cgt gcg tcc agg ggc
121  ggc taa tgc ccc tca cgc tgt cta cgc tgc tgc aac cgg gcc gca tct gga cgg ggc gcc
181  gcg cgg cgg agc cga cgc cgg gcc aca atg ctg ctt gga gcc tct ctg gtg ggg gtg ctg
      M L L G A S L V G V L
241  ctg ttc tcc aag ctg gtg ctg aaa ctg ccc tgg acc cag gtg gga ttc tcc ctg ttg ttc
      L F S X L V L K L P W T Q V G F S L L F
301  ctc tac ttg gga tct ggc ggc tgg cgc ttc atc cgg gtc ttc atc aag acc atc agg cgc
      L Y L G S G G W R F I R V F I K T I R R
361  gat atc ttt ggc ggc ctg gtc ctc ctg aag gtg aag gca aag gtg cga cag tgc ctg cag
      D I F G G L V L L K V K A K V R Q C L Q
421  gcg cgg cgg aca gtc ccc att ttg ttt gcc tct acc gtt cgg cgc cac ccc gac aag acg
      E R R T V P I L F A S T V R R H P D K T
481  gcc ctg atc ttc gag ggc aca gat acc cac tgg acc ttc cgc cag ctg gat gag tac tca
      A L I F E G T D T H W T F R Q L D E Y S
541  agc agt gta gcc aac ttc ctg cag gcc cgg ggc ctg gcc tgg ggc gat gtg gct gcc atc
      S S V A N P L Q A R G L A S G D V A A I
601  ttc atg gag aac cgc aat gag ttc gtg ggc cta tgg ctg ggc atg gcc aag ctc ggt gtg
      F M E N R N E F V G L W L G M A K L G V
661  gag gca gcc ctc atc aac acc aac ctg cgg cgg gat gct ctg ctc cac tgc ctc acc acc
      E A A L I N T N L R R D A L L H C L T T
721  tgc cgc gca cgg gcc ctt gtc ttt ggc agc gaa atg gcc tca gcc atc tgt gag gtc cat
      S R A R A L V F G S E M A S A I C E V H
781  gcc agc ctg gac ccc tgc ctc agc ctc ttc tgc tct ggc tcc tgg gag ccc ggt ggc gtg
      A S L D P S L S L F C S G S W E P G A V
841  cct cca agc aca gaa cac ctg gac cct ctg ctg aaa gat gct ccc aag cac ctt ccc agt
      P P S T E H L D P L L K D A P K H L P S
901  tgc cct gac aag ggc ttc aca gat aaa ctg ttc tac atc tac aca tcc ggc acc aca ggg
      C P D K G F T D K L F Y I Y T S G T T G
961  ctg ccc aag gcc cgc atc gtc gtc cag agc agt tat tac cgc atg gct gcc ctg gtg tac
      L P K A A I V V H S R Y Y R M A A L V Y
1021  tat gga ttc cgc atc cgg ccc aac gac atc gtc tat gac tgc ctc ccc ctc tac cac tca
      Y G F R M R P N D I V Y D C L P L Y H S
1081  gca gga aac atc gtc gga atc ggc cag tgc ctg ctg cat ggc atg acg gtg gtg att cgg
      A G N I V G I G Q C L L H G M T V V I R
1141  aag aag ttc tca gcc tcc cgg ttc tgg gac gat tgt atc aag tac aac tgc acg att gtg
      K K F S A S R F W D D C I K Y N C T I V
1201  cag tac att ggt gaa ctg tgc cgc tac ctc ctg aac cag cca cgc cgg gag gca gaa aac
      Q Y I G E L C R Y L L N Q P P R E A E N
1261  cag cac cag gtc cgc atc gca cta ggc aat ggc ctc cgg cag tcc atc tgg acc aac ttt
      Q H Q V F M A L G N G L R Q S I W T N F
1321  tcc agc cgc ttc cac ata ccc cag gtc gct gag ttc tac ggg gcc aca gag tgc aac tgt
      S R F R M I P Q V A E F Y G A T E C N C
1381  agc ctg ggc aac ttc gac agc cag gtc ggg gcc tgt ggt ttc aat agc cgc atc ctg tcc
      S L G N F L G S Q V G A C G F N S R I L S
1441  ttc gtc tac ccc atc cgg ttg gta cgt gtc aac gag gac acc atg gag ctg atc cgg ggg
      F V Y P I R L V R V N E D T M E L I R G
1501  ccc gac ggc gtc tgc att ccc tgc cag cca ggt gag cgg ggc cag ctg gtg ggc cgc atc
      P D G V C I P C Q P G E P G Q L V G R I
1561  atc cag aaa gac ccc ctg cgc cgc ttc gat ggc tac ctc aac cag ggc gcc aac aac aag
      I Q K D P L R R F D G Y L N Q G A N N K
1621  aag att gcc aag gat gtc ttc aag aag ggc gac cag gcc tac ctt act ggt gat gtc ctg
      K I A K D V F K K G D Q A Y L T G D V L
1681  gtg atg gac gag ctg ggc tac ctg tac ttc cga gac cgc act ggg gac acg ttc cgc tgg
      V M D E L G Y L Y F R D R T G D T F R W
1741  aaa ggt gag aac gtc tcc acc acc gag gtc gaa ggc aca ctc agc cgc ctg ctg gac atg
      K G E N V S T T E V E G T L S R L L D M
1801  gct gac gtc gcc gtc tat ggt gtc gag gtc cca gga acc gag ggc cgg gcc gga atg gct
      A D V A V Y G V E V P G T E G R A G M A
1861  gct gtc gcc agc ccc act ggc aac tgt gac ctg gag cgc ttt gct cag gtc ttg gag aag
      A V A S P T G N C D L E R F A Q V L E K
1921  gaa ctg ccc ctg tat ggc cgc ccc atc ttc ctg cgc ctc ctg cct gag ctg cac aaa aca
      E L P L Y A R P I F L R L L P E L H K T
1981  gga acc tac aag ttc cag aag aca gag cta cgg aag gag ggc ttt gac cgg gct att gtc
      G T Y K F Q K T E L R K E G F D F A I V
2041  aaa gac cgc ctg ttc tat cta gat gcc cag aag ggc cgc tac gtc cgc ctg gac caa gag
      K D P L F Y L D A Q K G R Y V P L D Q E
2101  gcc tac agc cgc atc cag gca ggc gag gag aag ctg tga ttc ccc cca tcc ctc tga ggg
      A Y S R I Q A G E E K L
2161  cgg gcg gat gct gga tcc gga gcc cca ggt tcc gcc cca gag cgg tcc tgg aca agg cca
2221  gac caa agc aag cag ggc ctg gca cct cca tcc tga ggt gct gcc cct cca tcc aaa act
2281  gcc aag tga atc att gcc ttc cca acc ctt cca gag gct ttc tgt gaa agt ctc atg tcc
2341  aag ttc cgt ctt ctg ggc tgg gca ggc cct ctg gtt ccc agg ctg aga ctg acg ggt ttt
2401  ctc agg atg atg tct tgg gtc agg gta ggg aga gga caa ggg gtc acc gag ccc ttc cca
2461  gag agc agg gag ctt ata aat gga acc aga gca gaa gtc ccc aga ctc agg aag tca aca
2521  gag tgg gca ggg aca gtc gta gca tcc atc tgg tgg cca aag aga atc gta gcc cca gag
2581  ctg ccc aag ttc act ggg ctc cac ccc cac ctc cag gag ggg agg aga gga cct gac atc
2641  tgt agg tgg ccc ctg atg ccc cat cta cag cag gag gtc agg acc acg ccc ctg gcc tct
2701  ccc cac tcc ccc atc ctc ctc cct ggg tgg ctg cct gat tat ccc tca ggc agg gcc tct
2761  cag tcc ttg tgg gtc tgt gtc acc tcc atc tca gtc ttg gcc tgg cta tga ggg gag gag
2821  gaa tgg gag agg ggg ctc agg ggc caa taa act ctg cct tga gtc ctc cta aaa aaa aaa
2881  aaa aaa aaa aaa aaa aaa aaa aaa ggg cgg cgg c

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Figure 27

Protein sequence 646 a.a. MRAPGAGAASVV ... VYTRICSGAFAL

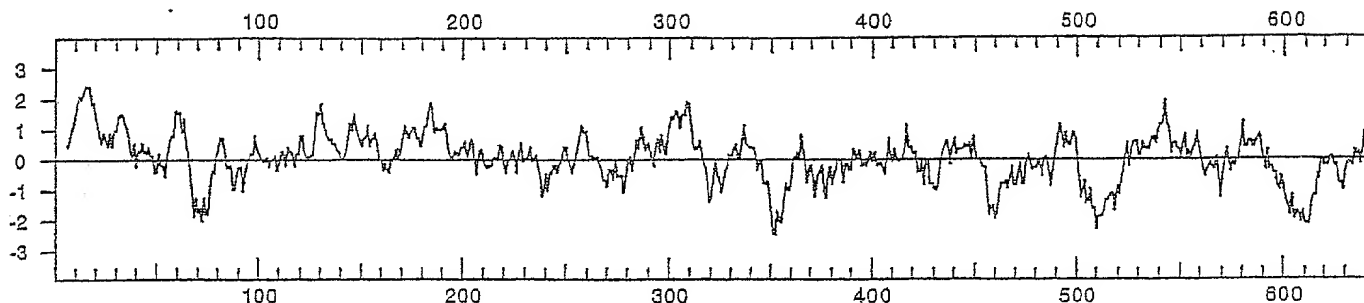


Figure 28A

Protein sequence 646 a.a. MRAPGAGAASVV ... VYTRICSGAFAL

646 Amino Acids MW : 71062 Dalton

	n	n(%)	MW	MW(%)
A ala alanine	64	9.9	4546	6.4
C cys cysteine	15	2.3	1545	2.2
D asp aspartic acid	30	4.6	3450	4.9
E glu glutamic acid	31	4.8	4000	5.6
F phe phenylalanine	29	4.5	4264	6.0
G gly glycine	63	9.8	3592	5.1
H his histidine	13	2.0	1781	2.5
I ile isoleucine	29	4.5	3279	4.6
K lys lysine	22	3.4	2818	4.0
L leu leucine	77	11.9	8707	12.3
M met methionine	11	1.7	1441	2.0
N asn asparagine	15	2.3	1710	2.4
P pro proline	29	4.5	2814	4.0
Q gln glutamine	25	3.9	3201	4.5
R arg arginine	49	7.6	7648	10.8
S ser serine	33	5.1	2872	4.0
T thr threonine	27	4.2	2728	3.8
V val valine	51	7.9	5052	7.1
W trp tryptophan	9	1.4	1674	2.4
X ukw unknown	-	-	-	-
Y tyr tyrosine	24	3.7	3913	5.5
Z --- STOP	-	-	-	-

Figure 28B

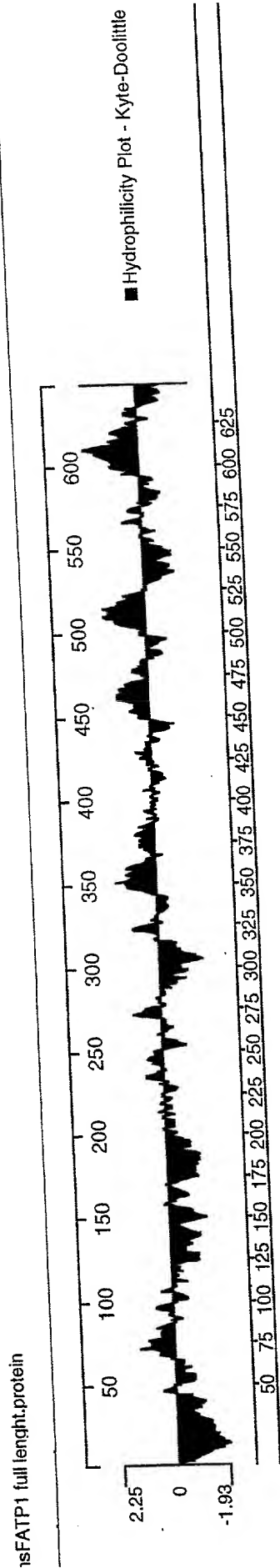


Figure 28C

hsFATP4.pep -> KD Hydrophobicity <11/1>

Protein sequence 643 a.a. MLLGASLVGVLL ... AYSRIQAGEEKL

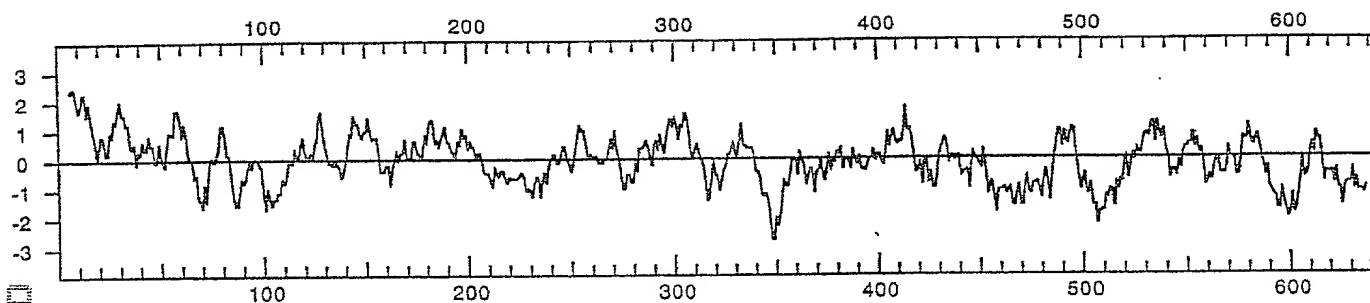


Figure 29A

hsFATP4.pep -> A. A. Usage

Protein sequence 643 a.a. MLLGASLVGVLL ... AYSRIQAGEEKL

643 Amino Acids MW : 72018 Dalton

		n	n(%)	MW	MW(%)
A	ala alanine	46	7.2	3267	4.5
C	cys cysteine	16	2.5	1648	2.3
D	asp aspartic acid	33	5.1	3795	5.3
E	glu glutamic acid	33	5.1	4258	5.9
F	phe phenylalanine	34	5.3	5000	6.9
G	gly glycine	54	8.4	3079	4.3
H	his histidine	12	1.9	1644	2.3
I	ile isoleucine	30	4.7	3392	4.7
K	lys lysine	31	4.8	3970	5.5
L	leu leucine	76	11.8	8594	11.9
M	met methionine	12	1.9	1572	2.2
N	asn asparagine	21	3.3	2394	3.3
P	pro proline	31	4.8	3008	4.2
Q	gln glutamine	23	3.6	2945	4.1
R	arg arginine	45	7.0	7024	9.8
S	ser serine	35	5.4	3046	4.2
T	thr threonine	32	5.0	3233	4.5
V	val valine	46	7.2	4557	6.3
W	trp tryptophan	8	1.2	1488	2.1
X	ukw unknown	-	-	-	-
Y	tyr tyrosine	25	3.9	4076	5.7
Z	--- STOP	-	-	-	-

Figure 29B

hsFATP4 full length, protein

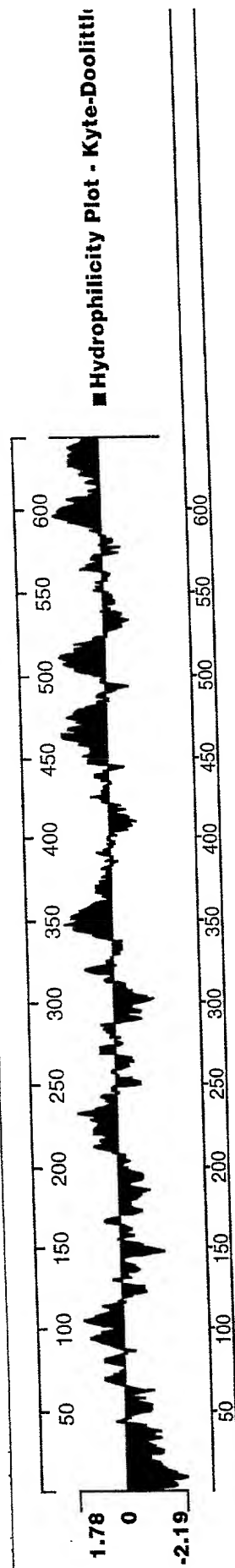


Figure 29C

1 ATGCCGGCTCCGGGTGCGGGCGCGGCCTGGTGGTCTCTGGCTGGCGGCTGT hFATP1con.seq ORF
1 ATGCCGGCTCCGGGTGCGGGCGCGGCCTGGTGGTCTCTGGCTGGCGGCTGT mFATP1.seq ORF (from genomic)

51 GTGGCTGCTGGGGGCGCGGTGGACCTGGAGCGCGCGAGCGGGCTCGGGCG hFATP1con.seq ORF
51 TTGGCTTCTGGGGGAGTCCGCTGGACCTGGAGCGCGCGGGCGGGCTGGTGG mFATP1.seq ORF (from genomic)

101 TGTACCTGGGCAAGGGCGGGCTGGGGCTTCCTGGC CATGGCTCTGCAAGAGC hFATP1con.seq ORF
101 TGTACCTGGGCTGGGGCGGGCTGGGGCTTCCTGGC TATGGCTCTGCAAGAGC mFATP1.seq ORF (from genomic)

151 GCGAGGGCGAGACCTCTCGGTCTCTCTGGTGGTGGATCGCGGTGGCGCTGGGA hFATP1con.seq ORF
151 GCGAGGGCGAGACCTCTCTGGTCTCTCTGGTGGTGGATCGCGGTGGCGCTGGGA mFATP1.seq ORF (from genomic)

201 GGTGGCGGGGCGACAGCTGGCGGGCCACACCATCCCGCGCATCTTTCAGG hFATP1con.seq ORF
201 GGTGGCGAGGACAGCGGGCGAGCAGGAGACAGCATCCCGTGCATCTTTCAGG mFATP1.seq ORF (from genomic)

251 GGGTAGTGTAGCGGAGCGCCGAGCGGGCTGGCGGTGGTGGATGGCGGGAGCC hFATP1con.seq ORF
251 CTGGGGCCGGGGCGAGAACAGAGCGGGCTGGGACTGGCTGGACGGCAAGTAGT mFATP1.seq ORF (from genomic)

301 GCGGAGTGGCTGGACCTTTCGCGGAGCTGGAGCGGCTACTCGCAATGGGGTAGG hFATP1con.seq ORF
301 GGTATACTGGTGGACCTTTCGCGGAGCTGGAGCACCTACTCGCAATGGGGTAGG mFATP1.seq ORF (from genomic)

351 CAAGCTCTTCGCGGAGCTGGGGCTTCGGGCTGGGGCACTGGGTGGGCACTC hFATP1con.seq ORF
351 CAAGCTCTTCGCGGAGCTGGGGCTTATGGAGGAGGGCGATGGGTGGGCTGGTGG mFATP1.seq ORF (from genomic)

401 TCGTGGAGGGCGGGCGGAGCTCTGGGGCTGGTGGCTGGGCTGGGCGCAAG hFATP1con.seq ORF
401 TCGTGGAGGGCGGGCGGAGCTCTGGGGCTGGTGGCTGGGCGTGGGCGCAAG mFATP1.seq ORF (from genomic)

451 GCGGGCATGGAGGGCGGGCTGGGTGGTGGCTGGTGGCTGGTGGCTGGTGG hFATP1con.seq ORF
451 GCGGGCTGGGGTGGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGG mFATP1.seq ORF (from genomic)

501 GGGCTTCTGGCTGGGGACCTCGGGCGCTAAGGGCGGTGATCTTTGGAGGAG hFATP1con.seq ORF
501 GGGCTTCTGGCTGGGGACCTCGGGCGCTAAGGGCGGTGATCTTTGGAGGAG mFATP1.seq ORF (from genomic)

551 AAGTGTGGCGGGGGTGGCGGAAGTGGAGCGGGCATCTGGGGGAAAGTTTG hFATP1con.seq ORF
551 AAGTGTGGCGGGGGTGGCGGGAGTGGAGCGGGCATCTGGGGGAAAGTTTG mFATP1.seq ORF (from genomic)

601 ATCAAGTTCTGCTCTGGAGACTTGGGGGGCGGAGGGCATCTTGGCGGAGAC hFATP1con.seq ORF
601 CTCAAGTTCTGCTCTGGAGACTTGGGGGGCTGGAGAGGAGCTTGGCGGAGAC mFATP1.seq ORF (from genomic)

651 CCACTCTCTGGACCGCGCTCTGAAGGAGGGCTTACTGGCCCGCTGGGCA hFATP1con.seq ORF
651 GCACTCTCTGGACCGCGCTCTGAAGGAGGGCTTACTGGCCCGCTGGGCA mFATP1.seq ORF (from genomic)

701 AGATCGGCAGGAGGGGATGGAGGATCTCTTTCTTACATCTACAGGTGG hFATP1con.seq ORF
701 AAGCCCCAGGAGGGGATGGAGGATCTCTTTCTTACATCTTACTTGGT mFATP1.seq ORF (from genomic)

751 GGGACCAACCGGGCTGGCCCAAGGCTGGCATCTCTGGTGCACAGAGGTA hFATP1con.seq ORF
751 GGGACCAACCGGGCTGGCCCAAGGCTGGCATCTCTGGTGCACAGAGGTA mFATP1.seq ORF (from genomic)

801 CCGCATGGGAGGGCTTGGGGACCA CGGCTACCGCATGGAGGGGGTGA hFATP1con.seq ORF
801 CCGCATTGGTGGGGTGGGGACCA TTCCCTAGAGGATGGGTTCGGCGGATG mFATP1.seq ORF (from genomic)

851 TGGCTGATGAGTGGCTGGCCCTGTGTACCACTGGGAGGAAACATCATCGG hFATP1con.seq ORF
851 TGGCTGATGAGTGGCTGGCCCTGTGTACCACTGGGAGGAAACATCATCGG mFATP1.seq ORF (from genomic)

901 GTGGGGCAGTGTCTCATCTATGGGGCTGAGAGTCTCTCTCCGCAAGAAATT hFATP1con.seq ORF
901 GTGGGGCAGTGTCTCATCTATGGGGCTGAGAGTCTCTCTCCGCAAGAAATT mFATP1.seq ORF (from genomic)

951 CTCGGGACCGGGCTTGTGGGACGAGTGCATCAAGTACACTTGCACGGTGG hFATP1con.seq ORF
951 CTCGGGACCGGGCTTGTGGGACGAGTGCATCAAGTACACTTGCACGGTGG mFATP1.seq ORF (from genomic)

1001 TTAGTACATCGGGGA GATCTGGCGCTACCTGGCTGAAGCAGCGGGTGG hFATP1con.seq ORF
1001 TTAGTACATAGGTGA AATCTGGCGCTACCTGGCTGAAGCAGCGGGTGG mFATP1.seq ORF (from genomic)

1051 GAGCGGGAGGGGACACCGCGTGGCGCTGGCGGTGGGAA CGGGGTGGG hFATP1con.seq ORF
1051 GAGCTGGGAGCAAGGACACCGCGTGGCGCTGGCGGTGGGAA TGGGGTGGG mFATP1.seq ORF (from genomic)

1101 TCTGGCATCTGGGAGGAGTTCAGCGAGCGCTGGCGGTAGGCCAATGG hFATP1con.seq ORF
1101 GCGAGCATCTGGGAGGAGTTCAGCGAGCGCTGGCGGTAGGCCAATGG mFATP1.seq ORF (from genomic)

1151 GGGAGTTCTAGGGGCGCACCGAGTGGCACTGCAAGTATGGCAACATGGAC hFATP1con.seq ORF
1151 GCGAGTTCTAGGGGCGCACCGAGTGGCACTGCAAGTATGGCAACATGGAC mFATP1.seq ORF (from genomic)

1201 GCGAAGGTGGGGCTGGCTGGTGTTCACAAAGCGCGCATCTGGCCCACTGGTA hFATP1con.seq ORF
1201 GCGAAGGTGGGGCTGGCTGGTGTTCACAAAGCGCGCATCTGGCCCACTGGTA mFATP1.seq ORF (from genomic)

1251 GCGCATCGGGCTGGTGGTGAAGGTCAATGAGGAGAAC AATGGAGCTGGCTGGGG hFATP1con.seq ORF
1251 GCGCATCGGGCTGGTGGTGAAGGTCAATGAGGAGAAC AATGGAGCTGGCTGGGG mFATP1.seq ORF (from genomic)

1301 ATGCCAGGGGGCTGTGATCCCTGGCGAGGGCGGGAGGCTGGGGCTCTT hFATP1con.seq ORF
1301 ACTGGAGAGGGGGCTGTGATCCCTGGCGAGGGCGGGAGGCTGGGGCTCTT mFATP1.seq ORF (from genomic)

FIG. 30A

1351 GTGGGTTCAGATCAACCAACAGGACCC GCTGCGCCGCTTCGATGGCTATGT hFATPlcon.seq ORF
1351 GTGGGCCAGATCAACCAACAGGACCC TCTGCGGCGTTCGATGGCTATGT mFATPl.seq ORF (from genomic)

1401 CAGCGAGAGCGCCACCAACAGGAGAAATCGCCACACAGCCTCTTCACCAAGG hFATPlcon.seq ORF
1401 TACTGACAGTGCACCAACAGGAGAAATCGCCACACAGCCTCTTCACCAAGG mFATPl.seq ORF (from genomic)

1451 GCGACAGCGCCCTACCTCTCAGGTGAAGTGGCTAGTCAATGGATGAGCTGGG hFATPlcon.seq ORF
1451 GCGATAGCGCCCTACCTCTCAGGTGAAGTGGCTAGTCAATGGATGAGCTGGG mFATPl.seq ORF (from genomic)

1501 TACATGTACTTCCGGGACCCGTAGCCGGGAGACCTTCGGCTGGGGAGGGGA hFATPlcon.seq ORF
1501 TACATGTATTTCCGTGACCCGAGCGGGGACACCTTCGGCTGGGGAGGGGA mFATPl.seq ORF (from genomic)

1551 GAACCTCTCCACCAACGAGGCTGGAGGGCGGTGGTCAAGCCGCTGCTGGGG hFATPlcon.seq ORF
1551 GAACCTCTCCACCAACGAGGCTGGAGAGCGGTGGTCAAGCCGCTGCTGGGG mFATPl.seq ORF (from genomic)

1601 AGACAGACCTTCCCTCTATATGGGGTGGCTCTCCAGGAGTGGAGGGTAG hFATPlcon.seq ORF
1601 AGACAGACCTTCCCTCTATATGGGGTGGCTCTCCAGGAGTGGAGGGTAG mFATPl.seq ORF (from genomic)

1651 GCAAGGATGGGGGGGGGTCGGAGAGCCCCACAGCCTGCTGGAGCCCAAGG hFATPlcon.seq ORF
1651 GCAAGGATGGGGGGGGGATCCGAGAGTCCCGACAGCCAGTGGAGCCCAAGG mFATPl.seq ORF (from genomic)

1701 GATATACCAAGGAGCTGCAGAGGGTGGTGGCACTATGGCTCGGGCCATCT hFATPlcon.seq ORF
1701 GATATACCAAGGAGCTGCAGAGGGTGGTGGCACTATGGCTCGGGCCATCT mFATPl.seq ORF (from genomic)

1751 TGGCTGGCTCTCTCTGGCCCAAGGTGGACACCCACAGCCACCTTCAAGATGAG hFATPlcon.seq ORF
1751 TGGCTGGCTCTCTCTGGCCCAAGGTGGATACCCACAGCCACCTTCAAGATGAG mFATPl.seq ORF (from genomic)

1801 AAGAGGAGGGCTGCAAGGAGAGGGGTTTGAGCCAGGCAGAGACCTCAGACC hFATPlcon.seq ORF
1801 AAGAGGAGGGCTGCAAGGAGAGGGGTTTGAGCCAGGCAGAGACCTCAGACC mFATPl.seq ORF (from genomic)

1851 GCTCTTCTCTCTCTGGAGCCTGAGAGCCAGCCAGTACCCTGAGCTTAAATGAG hFATPlcon.seq ORF
1851 GCTCTTCTCTCTCTGGAGCCTGAGAGCCAGCCAGTACCCTGAGCTTAAATGAG mFATPl.seq ORF (from genomic)

1901 CAGTCTACATTCGCACTCTCTCGGCGCCCTTCGGCTCTCTGA hFATPlcon.seq ORF
1901 GAGTCTACATTCGCACTCTCTCGGCGCCCTTCGGCTCTCTGA mFATPl.seq ORF (from genomic)

Decoration 'Decoration #1': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

FIG. 30B

1	100	G T T C T C C A A G C T G G T G G T A A A C T G C C C T G A C C C A G G T G G A T T C C C T G T T G T T C	hsFATP4
1	101	G T T G G G T C C A A G C T A G T G C T G A A G G T C C C C T G A C C C A G G T G G A T T C C C T G T T G T T C	nmFATP4
61	61	C C T A A T T G G G A A C T G G C G G C G G G C C T T C A T C G G G G T C T T C A T C A A G A C C A T C A G C C G C	hsFATP4
61	62	C C T A A T T G G G G T T G T G G T G G G T G G T T T C A T C G G G G T C T T C A T C A A G A C C A T C A G C C G C	nmFATP4
121	121	G A T A T G T T T G C C G C C T G G T C C T C C T G A G G T G A A G G A A A G C T G C G A A S T G C C T G G A G	hsFATP4
121	122	G A T A T C C T T T G C T G C A T G C T G C C C T G A G G T G A A G G A A A G C T G C G A A S T G C C T G G A G	nmFATP4
181	181	G A G C G G C G G A C A C T G C C C A T T T T T T T G C C C T C C G T T C G G C G C C A G C C C G A A G A C G	hsFATP4
181	182	G A G C G G A A A G C G G C C C G C T G C C T T G C T T G A T G G T A G A G C G C C A C C G G A C A A G A C A	nmFATP4
241	241	G C C C T G A T C T T C G A G G G C C C A T T C C A C T G C C C T T C C G C A G C T G A T G A T A C C C	hsFATP4
241	242	G C C C T G A T T T T C G A G G G C C C A T T C C A C T G C C C T T C C G C A G C T G A T G A T A C C C	nmFATP4
301	301	A C C A T T G T A C C A A T T C C T G C A G G C C C G G G C C T G G G G G G C G T G G G G C C C C A T C	hsFATP4
301	302	A C C A T T G T G C C A A T T C C T G C A G G C C C G G G C C T G G G G G G C G T G G G G C C C C A T C	nmFATP4
361	361	T T C A T G G A G A A C C G A A T G A G T T C T G G G C C T A T G G G T G G C C A T G G C C A A G A T C G G T G T G	hsFATP4
361	362	T T T A T G G A A A C C G A A T G A G T T C T G G G C C T A T G G G T G G C C A T G G C C A A G A T C G G G C G T G	nmFATP4
421	421	G A G G A G G C C T C A T C A A C A C C A A C C T G C G G G G G A T G T T G G T C C A C T C C C T C A C C A C	hsFATP4
421	422	G A G G C G G G T T C A T C A A C A C C A A C C T T A G G C G G A T G C C G G G C C A C T C C C T C A C C A C	nmFATP4
481	481	G C G C G G G G G C C C T G T G T T T T G C C C C G A A A T G G C C C A G C C A T T T G T G A G G T C C A T	hsFATP4
481	482	A A A G G G A A A G G T C T C A T T T T T G C C C C T G A G A T G G C C C A G C C A T T T G T G A G A T C C A T	nmFATP4
541	541	C G C C C G G A C C C C T G G T A C C T T C T T C T G C T T G C C C C T G G G A G G C G G T G G G G T G	hsFATP4
541	542	T A G C C G G A G C C C A C A S T T A G C C T C T T T G G T C T G C A T C C T G G A G G C C A G C A A A C T G	nmFATP4
601	601	C C T C C A A C C C C A A C C C T G G A G C C T G G T G A A A G A T G C T C C A A G C A C C T T C C A C C	hsFATP4
601	602	C G T C A C C A C C C A A C C C T G G A G C C T G T T T G G A A G A T G C C C G A A A G A C C T T C C A C C	nmFATP4
661	661	T G C C C T G A C A C C C C C A C C C A C C A C C T G T T G A A A G A T G C C C A A G C A C C T T C C A C C	hsFATP4
661	662	C A C C C A G A C A C C C C C A C C C A C C A C C T G T T G A A A G A T G C C C A A G C A C C T T C C A C C	nmFATP4
721	721	G G C C A A G G C C G C C C C G T C G T G C A C A G G C A G T A T T A C C C A T G G C C G C C T G G T G T A C	hsFATP4
721	722	A C C C A A A G C C T G C C C T T G T G T G C A C A G G C A G T A T T A T C C T A T G C C T T C C T G C G T G T A C	nmFATP4
781	781	T T G G A T T C C C C A T G C C C C C A C C A C C C C C A T G A C T G C C C C C C C C C T C A C C C T C A	hsFATP4
781	782	T A T G G A T T C C C C A T G C C C C C A C C A C C C C C A T G A C T G C C C C C C C C C T C A C C C T C A	nmFATP4
841	841	- T G A C C A A C A T C C T G G C A A C C G G C C C C C C T G C T G C C T G G C A T C C G T G G T G A T T C C	hsFATP4
841	842	A C C A G G A A C A T C C T G G C A A C C G G C C C C C C T G C T G C C T G G C A T C C G T G G T G A T T C C	nmFATP4
900	900	G A G A A A T T C C A G C C T C C C G T T C T G G G A C G A T T G A T C A A G A C A C C T G C C G A T T G T	hsFATP4
900	901	G A G A A A T T C C A G C C C C C C C C T T C T G G G A C G A T T G A T C A A G A C A C C T G C C G A T T G T	nmFATP4
960	960	G G G T A C C T G C T G A C G G G C C G C C C T C G A A C C A C C C C C G G G G G A G C A A A A	hsFATP4
960	961	A C A G T A C C T G C T G A C G G G C C G C C C T C G A A C C A C C C C C G G G G G A G C A A A A	nmFATP4
1020	1020	C C A B C A C C A G C C T G C C A T G G C A C A G C A A T G C C C T C G G C A G T C C A T C T G G A C C A C C T	hsFATP4
1020	1021	T G G C A C A A G C C T G C C A T G G C A C A G C A A T G C C C T C G G C A G T C C A T C T G G A C C A C C T	nmFATP4
1080	1080	T T C A G G C C G C C C C A A A C C C A G G T G C C T A G T C A C C G G G C A A A A G G G C A A C T G	hsFATP4
1080	1081	C T C A G G C C G C C C C A A A C C C A G G T G C C T A G T C A C C G G G C A A A A G G G C A A C T G	nmFATP4
1140	1140	T A G C C T G C C A C C C C A C C C A C C C A C C T G G G G C C T G T T T T A A T G C C C A T C C T G T G C	hsFATP4
1140	1141	T A G C C T G C C A C C C C A C C C A C C C A C C T G G G G C C T G T T T T A A T G C C C A T C C T G T G C	nmFATP4
1200	1200	C T T C G T G T C C C C T G C G T T G G T A C C T G C A A C G A G G A C A C C A T G C G C T G C C G G G	hsFATP4
1200	1201	C T T T G T T T A C C C T T G C T T T G C T A C C T G C A A C G A G G A C A C C A T G C G C T G C C G G G	nmFATP4
1260	1260	G C C C G A C C C C G C C T G C A T T G C C T G C C G C A A G G A G G C G G C A G G T G G T G G G C C G C A T	hsFATP4
1260	1261	A C C C G A T G C A A G C C T G C A T T G C C T G C C G C A A G G A G G C G G C A G G T G G T G G G C C G C A T	nmFATP4
1320	1320	C A T C C A A A C G C C C C T G G G C C C C T T G C T G C C C C C A C C A C C C C C C C A A A A A	hsFATP4
1320	1321	C A T C C A A A C G C C C C T G G G C C C C T T T T G C C C G G C C C C A C C A C C C C C C A A A A A	nmFATP4
1380	1380	G A G A T T G C C C G G T G T C T C A A G A A G G G G A C C G C C T A C C T T A T G G T G T T G T G C T	hsFATP4
1380	1381	G A G A T T G C C C G G T G T C T C A A G A A G G G G A C C A C C T A C C T T A T G G T G T T G T G C T	nmFATP4
1440	1440	G G T G A T G A C G A G C C T G C C T A C C T T A G T T C C A G A C C C A C T G G G A A C C G T T C C C T G	hsFATP4
1440	1441	G G T G A T T G A T G A G C C T G C C T A C C T T A G T T C C A G A C C C A C T G G G A A C C G T T C C C T G	nmFATP4
500	500	G A A A G T G G A C C C G C	hsFATP4
500	501	G A A A G T G G A C C C G C	nmFATP4
560	560	G G T G A C C T G C	hsFATP4
560	561	G G T G A C C T G C	nmFATP4

Figure 3/A

1620	TGC TGT GGG CAG CCC CTA	CTG GAA CTT GTG ACG TGG AG	CGG CTT GAC TCT GTT TTT GAG	GAT	hsFATP4	
1620	TGC CCG TGG AAT TCG CTA	CTA CCA CCG TGG ACG TGG AG	AGG CTT TGC ACG GAC CTT CAA	AGA	nmFATP4	
1680	GCA AAT GGG CCG TAT TGG	GCG CCG CTT CTT CTT GCG	CTC CTG CCG TGG GCT TCG ACA	ATA	hsFATP4	
1680	GCG GCT GCG TCT TCA TAC	CGC CCG CTT CTT TCG CCG	TTC TTT CCG CTT GCT TGA CAA	GAT	nmFATP4	
1740	ACG AAC GAT AC CAG TTC CAG AAG ACG AG	CTA CCG GAG GGG GCG CTT TCG CCG	GGA ATG C	hsFATP4		
1740	ACG GAC CTT TCA CTT CCA CAG GCA CAG AT	CTG GCG AAG GAG GCG CTT TGA CCG	ATC GTT GGT	nmFATP4		
1800	GAA AGA CCG CCG TGT TCT TACT	AGATTC	CTA CAG AGG CGC CCG TTT CCG	CCG GCT TGA CCG	AGA	hsFATP4
1800	GAA AAG CCG CCG TGT TCT TACT	GCA TGG CTG GAG AGG CTTGCTACGTTG	ACT GCA GCA GCA	GGA	nmFATP4	
1960	GCG CTT	CTG CCG CAG CAG CAG GCG AGG CAG CAG CTT			hsFATP4	
1960	GCG CTT	CTC CCG CAG CAG CAG GCG AGG CAG CAG CTT			nmFATP4	

Decoration 'Decoration #1': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

Figure 31B

1	M R A P G A G A S V V E H A L L W L G I E W T W S A A A L C A Y V G S G G R E L R I V C R T A R R D D F G D S V	hsFAT1pep
1	M R A P G A G T S S A S L A D D S F I G L E Y T W S A A A F C Y V A V G G G G R E L R I V C R T A R R D D F G D S V	mmFAT1pep
61	L L R V R E E E R E L Q R A G H T L R R P O A A V O R Q P E R L A L V D A G T G E E N T E A O D A S N A V A N L E	hsFAT1pep
61	L L R V R E E E R E R R A G D T L R C E P O A A R R Q P E R L A L V D A S S G I E W T F A S L T S N A V A N L E	mmFAT1pep
121	P O T G F A P C D V R I L E G F P E E G I W L G L A K A G M E A A L E N I E R E P T A C G G S G A I A I E	hsFAT1pep
121	P O T G F A P C D V V A V L E G R R E E G I W L G L A K A G V V A A G N N E R E R E P T A C C L G A S A A I E	mmFAT1pep
181	F G G E M V A D V A E V S G H L E K S I I K F C S G D L G E E G T P E D T H L D D L K R E A S T A P L A O I E S R G M	hsFAT1pep
181	Y G G E M A A A V A E V S E Q L G S L L R F C S G D L G E E S L T P E D T Q L E E P M A P A P T T P L A Q A E G K G M	mmFAT1pep
241	D D R L E V Y T S G T T G L P A A I V V H E R V Y E M A A F C H A M R M Q A A D V L V D C E P L Y H S A G N I I G	hsFAT1pep
241	D D R L E V Y T S G T T G L P A A I V V H E R V Y E M A A F C H S S M R A A D V L V D C E P L Y H S A G N I I M G	mmFAT1pep
301	G G C L E Y G L T V L R K K P S S S P E W D D C I V A C T S V Q A N C E L C H R E L K Q E L E E A E R R H R V R E	hsFAT1pep
301	V G G C V L E Y G L T V L R K K S A S R F F A D D C V K V N C T V Q A N C E L C H R E L R Q E L E D V E Q R H R V R E	mmFAT1pep
361	A V G N Q L R E A I N B E R E R E E V R Q I G E P Y C T E C N G S M A N M D G A V G S C G E N S R T L P H V A Y P T R	hsFAT1pep
361	A V G N Q L R E A I N B E R Q R E G V P O L G E E Y G A T E C N C S T I A N M D G K V G S C G E N S R T L T P V V Y P T R	mmFAT1pep
421	L Y K V N E D D T M E L L D D A Q G L C L E C Q A G E P G L L V G C I N Q O D P L R R E D G A V S E S A T S K P L A H S V	hsFAT1pep
421	L Y K V N E D D T M E P L L R S E Q L C L E C Q P G E R G L L V G C I N Q O D P L R R E D G A V S D S A T N I K K L A H S V	mmFAT1pep
481	S G G D S A Y L S G D V Y M D E L G Y M V T R D R S G D T E R W R G E N V S T T E A E G V A L S R L L G O D D V A V	hsFAT1pep
481	R I G G D S A Y L S G D V Y M D E L G Y M V T R D R S G D T E R W R G E N V S T T E V E A V L S R L L G O D D V A V	mmFAT1pep
541	G V A V P G V E G V A G M A V A D P H S L L D E N A I V O E L O K V L A P A R P I E L R L L P O V D T T G I P K L Q	hsFAT1pep
541	G V A V P G V E G V A G M A I A D P H S Q L D R N S M Q O E L O K V L A S A R P I E L R L L P O V D T T G I P K L Q	mmFAT1pep
601	K I R L Q R E G E E R O T S D R L P P L D I K Q G H Y L P N E A V Y T R Y G S G A A I I	hsFAT1pep
601	K I R L Q R E G E E R O T S D R L P P L D I K Q G R A V P L D E R Y H A R P A G D E S L I	mmFAT1pep

Decoration 'Decoration #2': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

Figure 32

005504-00260-005504

1	FPSKLVKRLPFWTQCPSTLIFVYGGCGWRFPPLKIKIIRCLFGGLVETLVVAVVRQCLO	hsFAT4p4ep
1	TGSAUVLSTPLVWUCPSLILLVYGGGWRFPPLVATLVVNDLFGGLMDELKVRTVVRVRYLO	mmFAT4p4ep
61	ERRRQVILIDRSTTRRSHPRPTALSPEDGDDTHWTFRCDBSVSSVYANFQAGGHAASDVAI	hsFAT4p4ep
61	ERRKIVRLIPLSSMQRHPRPKALPSPGDDTHWTFRCDBSVSSVYANFQAGGLASIGNVVL	mmFAT4p4ep
121	FMEANRNBFVGCWVGWAGVGAALNTNLRBDALVLCCTTPRRLRATVVGGSBMSDACEV	hsFAT4p4ep
121	FMEANRNBFVGLWVGWAGVGAALNTNLRBDALRHCTDPRKARATVVGSSMASPTCEI	mmFAT4p4ep
181	SSDSSGGLFCGGSWRGAIPSTETDEELKDAFKHLLCGDAGETDKRLVTVVRSCHD	hsFAT4p4ep
181	SPETTHSLDSSSWRPSSTVVSSTREHLDRLKDAFKHLLCGDAGETDKRLVTVVRSCHD	mmFAT4p4ep
241	LPRAIVVHSSRYRMALVYVYGERMRLNIDIVDGLPLVHLAGNIVIGCPHGHGTVVR	hsFAT4p4ep
241	LPKASIVHSSRYRMALVYVYGERMRLNIDIVDGLPLVHLAGNIVIGCPHGHGTVVR	mmFAT4p4ep
301	KKPSASRHHDDCKKYNCTIIVQVCGEPRLDLPQPLRNOIQARVCGWGLRQSTWVNI	hsFAT4p4ep
301	KKPSASRHHDDCKKYNCTIIVQVQGLDLCVYLDLPQPLRNRHKKVRLMGLNGLPQSTWVD	mmFAT4p4ep
361	SSRHHPCQVAEPVAGATPCNCSQDNLPSQVGAAGFNSGRITSEVYVETALLVRNEDTMELLRQ	hsFAT4p4ep
361	SSRHHPCQVAEPVAGATPCNCSQDNLPSRYGAAGFNSGRITSEVYVETALLVRNEDTMELLRQ	mmFAT4p4ep
421	PDGAGTPTQDGPEDGQGVCRITQKDFPRRHHGVNQGANNGKTLKDAFRRKGDQAVLTGDEL	hsFAT4p4ep
421	PDGAGTPTQDGPQSGQGVCRITQQDFRRRHHGVNQGANNGKTLNNDPRKKGDDQAVLTGDEL	mmFAT4p4ep
481	VMDPLGVLVRRDPTGDTLRRGCVSRVETEGTSSHSLDINDVAVVGVVYDGTGGRAGCV	hsFAT4p4ep
481	VMDPLGVLVRRDPTGDTLRRGCVSRVETEGTSSHSLHMDVAVVGVVYDGTGGRAGCV	mmFAT4p4ep
541	VASSTGNQDLERLQVIEKELPLIARPHFLRLDPLHRTGQYKFKQKTELRKRGFDFIAI	hsFAT4p4ep
541	VASRIINQDLERLQVIEKELPLIARPHFLRLDPLHRTGQYKFKQKTELRKRGFDFISV	mmFAT4p4ep
601	KDPLPLLDARQKRVPLDDESRDQGEER	hsFAT4p4ep
601	KDPLPLLDARQKRVPLDDESRDQGEER	mmFAT4p4ep

Operation 'Decoration #1': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

1. 1. The first
 2. 2. The second
 3. 3. The third
 4. 4. The fourth
 5. 5. The fifth
 6. 6. The sixth
 7. 7. The seventh
 8. 8. The eighth
 9. 9. The ninth
 10. 10. The tenth
 11. 11. The eleventh
 12. 12. The twelfth
 13. 13. The thirteenth
 14. 14. The fourteenth
 15. 15. The fifteenth
 16. 16. The sixteenth
 17. 17. The seventeenth
 18. 18. The eighteenth
 19. 19. The nineteenth
 20. 20. The twentieth
 21. 21. The twenty-first
 22. 22. The twenty-second
 23. 23. The twenty-third
 24. 24. The twenty-fourth
 25. 25. The twenty-fifth
 26. 26. The twenty-sixth
 27. 27. The twenty-seventh
 28. 28. The twenty-eighth
 29. 29. The twenty-ninth
 30. 30. The thirtieth
 31. 31. The thirty-first
 32. 32. The thirty-second
 33. 33. The thirty-third
 34. 34. The thirty-fourth
 35. 35. The thirty-fifth
 36. 36. The thirty-sixth
 37. 37. The thirty-seventh
 38. 38. The thirty-eighth
 39. 39. The thirty-ninth
 40. 40. The fortieth
 41. 41. The forty-first
 42. 42. The forty-second
 43. 43. The forty-third
 44. 44. The forty-fourth
 45. 45. The forty-fifth
 46. 46. The forty-sixth
 47. 47. The forty-seventh
 48. 48. The forty-eighth
 49. 49. The forty-ninth
 50. 50. The fiftieth
 51. 51. The fifty-first
 52. 52. The fifty-second
 53. 53. The fifty-third
 54. 54. The fifty-fourth
 55. 55. The fifty-fifth
 56. 56. The fifty-sixth
 57. 57. The fifty-seventh
 58. 58. The fifty-eighth
 59. 59. The fifty-ninth
 60. 60. The sixtieth
 61. 61. The sixty-first
 62. 62. The sixty-second
 63. 63. The sixty-third
 64. 64. The sixty-fourth
 65. 65. The sixty-fifth
 66. 66. The sixty-sixth
 67. 67. The sixty-seventh
 68. 68. The sixty-eighth
 69. 69. The sixty-ninth
 70. 70. The seventieth
 71. 71. The seventy-first
 72. 72. The seventy-second
 73. 73. The seventy-third
 74. 74. The seventy-fourth
 75. 75. The seventy-fifth
 76. 76. The seventy-sixth
 77. 77. The seventy-seventh
 78. 78. The seventy-eighth
 79. 79. The seventy-ninth
 80. 80. The eightieth
 81. 81. The eighty-first
 82. 82. The eighty-second
 83. 83. The eighty-third
 84. 84. The eighty-fourth
 85. 85. The eighty-fifth
 86. 86. The eighty-sixth
 87. 87. The eighty-seventh
 88. 88. The eighty-eighth
 89. 89. The eighty-ninth
 90. 90. The ninetieth
 91. 91. The ninety-first
 92. 92. The ninety-second
 93. 93. The ninety-third
 94. 94. The ninety-fourth
 95. 95. The ninety-fifth
 96. 96. The ninety-sixth
 97. 97. The ninety-seventh
 98. 98. The ninety-eighth
 99. 99. The ninety-ninth
 100. 100. The hundredth

Figure 33

050504-060200

hsFATP6

```
1 aac ggc aag taa gog caa cgc aat taa tgt gag tag ctc act cat tag gca ccc cag gct
61 tta cac ttt atg ctt ccg ggc tgc tat gtt gtg tgg aat tgt gag cgg ata cca att tca
121 cac agg aac cag cta tga cat gat tac gaa ttt aat acg act cac tat agg gaa ttt ggc
181 cct cga ggc caa gaa ttc ggc acg agg ggt gct gag ccc ctg cgc ggt ttc tgg tgc gta
241 gag act gta aat cgc tgc gct tct cag tca tca tca tcc cag ctt ttc ccg gct cga att
301 cag cct cca act caa gct cgc ggg aaa gac tac ctg aga gga gaa aag ctt ctg tcc ctg
361 gac ctt ctt ctg agg gtg gag tgc gag gct ccc tgc ttt cca gcc gcc cag tga ccc aag
421 ctt aat ctt cag cac cac ttg ggg cga cct ttt cgg tgc aaa cct acg att ctg ttt ctc
481 agg att cct ccc cat ccc gct tgc ccc cgg aaa agc tga caa gaa ctt cag gtg taa gcc
541 ctg agt agt gag gat ctg cgg tct cgg tgg aga gct gtg cct gga aga gaa gga cgc tgg
601 tgg ggg ctg aga tca gag ctg tct tct ggc cca gct gcc ccc atg ctt ctg tca tgg cta
M L L S W L
561 aca gtt cta ggg gct gga atg gtc gtc ctg cac ttc ttg cag aaa ctc ctg ttc cct tac
T V L G A G M V V L H F L Q K L L F P Y
721 ttt tgg gat gac ttc tgg ttc gtg ttg aag gtg gtg ctc att ata att cgg ctg aag aag
F W D D F W F V L K V V L I I I R L K K
781 tat gaa aag aga ggg gag ctg gtg act gtg ctg gat aaa ttc ttg agt cat gcc aaa aga
Y E K R G E L V T V L D K F L S H A K R
841 caa cct cgg aaa cct ttc atc atc tat gag gga gac atc tac acc tat cag gat gta gac
Q P R K P F I I Y E G D I Y T Y Q D V D
901 aaa agg agc aga gtc gcc cat gtc ttc ctg aac cat tcc tct ctg aaa aag ggg gac
K R S S R V A H V F L N H S S L K K G D
961 acg gtg gct ctg ctg atg agc aat gag ccg gac ttc gtt cac gtg tgg ttc ggc ctc gcc
T V A L L M S N E P D F V H V W F G L A
1021 aag ctg ggc tgc gtg gtg gcc ttt ctc aac acc aac att cgc tcc aac tcc ctc ctg aat
K L G C V A F L N T N I R S N S L L N
1081 tgc atc cgc gcc tgc ggg ccc aga gcc cta gtg gtg ggc gca gat ttg ctt gga acg gta
C I R A C G P R A L V V G A D L L G T V
1141 gaa gaa atc ctt cca agc ctc tca gaa aat atc agt gtt tgg ggg atg aaa gat tct gtt
E E I L P S L S E N I S V W G M K D S V
1201 cca caa ggt gta att tca ctc ctc aaa gaa aaa ctg agc acc tca cct gat gag ccc gtg cca
P Q G V I S L K E K L S T S F D E P V P
1261 cgc agc cac cat gtt gtc tca ctc ctc aag tct act tgt ctt tac att ttt acc tct gga
R S H H V V S L L K S T C L Y I F T S G
1321 aca aca ggt cta cca aaa gca gct gtg att agt cag ctg cag gtt tta agg ggt tct gct
T T G L P K A A V I S Q L Q V L R G S A
1381 gtc ctg tgg gct ttt ggt tgt act gct cat gac att gtt tat ata acc ctt cct ctg tat
V L W A F G C T A H D I V Y I T L P L Y
1441 cat agt tca gca gct atc ctg gga att tct gga tgt gtt gag ttg ggt gcc act tgt gtg
H S S A A I L G I S G C V E L G A T C V
1501 tta aag aag aaa ttt tca gca agc cag ttt tgg agt gac tgc aag aag tat gat gtg act
L K K K F S A S Q F W S D C K K Y D V T
1561 gtg ttt cag tat att gga gaa ctt tgt cgc tac ctt tgc aaa caa tct aag aga gaa gga
V F Q Y I G E L C R Y L C K Q S K R E G
1621 gaa aag gat cat aag gtg cgt ttg gca att gga aat ggc ata cgg agt gat gta tgg aga
E K D H K V R L A I G N G I R S D V W R
1681 gaa ttt tta gac aga ttt gga aat ata aag gtg tgt gaa ctt tat gca gct acc gaa tca
E F L D R F G N I K V C E L Y A A T E S
1741 agc ata tct ttc atg aac tac act ggg aga att gga gca att ggg aga aca aat ttg ttt
S I S F M N Y T G R I G A I G R T N L F
1801 tac aaa ctt ctt tcc act ttt gac tta ata aag tat gac ttt cag aaa gat gaa ccc atg
Y K L L S T P D L I K Y D F Q K D E P M
1861 aga aat gag cag ggt tgg tgt att cat gtg aaa aaa gga gaa cct gga ctt ctc att tct
R N E Q G W C I H V K K G E P G L L I S
1921 cga gtg aat gca aaa aat ccc ttc ttt ggc tat gct ggg cct tat aag cac aca aaa gac
R V N A K N P F F G Y A G P Y K H T K D
1981 aaa ttg ctt tgt gat gtt ttt aag aag gga gat gtt tac ctt aat act gga gac tta ata
K L L C D V F K K G D V Y L N T G D L I
2041 gtc cag gat cag gac aat ttc ctt tat ttt tgg gac cgt act gga gac act ttc aga tgg
V Q D Q D N F L Y F W D R T G D T F R W
2101 aaa gga gaa aat gtc gca acc act gag gtt gct gat gtt att gga atg ttg gat ttc ata
K G E N V A T T E V A D V I G M L D F I
2161 cag gaa gca aac gtc tat ggt gtg gct ata tca ggt tat gaa gga aga gca gga atg gct
Q E A N V Y G V A I S G Y E G R A G M A
2221 tct att att tta aaa cca aat aca tct tta gat ttg gaa aaa gtt tat gaa caa gtt gta
S I I L K P N T S L D L E K V Y E Q V V
2281 aca ttt cta cca gct tat gct tgt cca cga ttt tta aga att cag gaa aaa atg gaa gca
T F L P A Y A C P R F L R I Q E K M E A
2341 aca gga aca ttc aaa cta ttg aag cat cag ttg gtg gaa gat gga ttt aat cca ctg aaa
T G T F K L L K H Q L V E D G F N P L K
2401 att tct gaa cca ctt tac ttc atg gat aac ttg aaa aag tct tat gtt cta ctg acc agg
I S E P L Y F M D N L K K S Y V L L T R
2461 gaa ctt tat gat caa ata atg tta ggg gaa ata aaa ctt taa gat ttt tat atc tag aac
E L Y D Q I M L G E I K L *
2521 ttt cat atg ctt tct tag gaa gag tga gag ggg ggt ata tga ttc ttt atg aaa tgg gga
2581 aag gga gct aac att aat tat gca tgt act ata ttt cct taa tat gag aga taa ttt ttt
2641 aat tgc ata aga att tta att tct ttt aat tga tat aaa cat tag ttg att act ctt ttt
2701 atc tac ttg gag att cag tgc ata act aag tat ttt cct taa tac taa aga ttt taa ata
2761 ata aat agt ggc tag cgg ttt gga caa tca cta aaa atg tac ttt cta ata agt aaa att
2821 tct aat ttt gaa taa aag att aaa ttt tac tga aaa aaa aaa aaa aaa aaa ttt ggc
2881 gcc gc
```

Figure 34

Protein sequence 619 a.a. MLLSWLTVLGAG ... LYDQIMLGEIKL

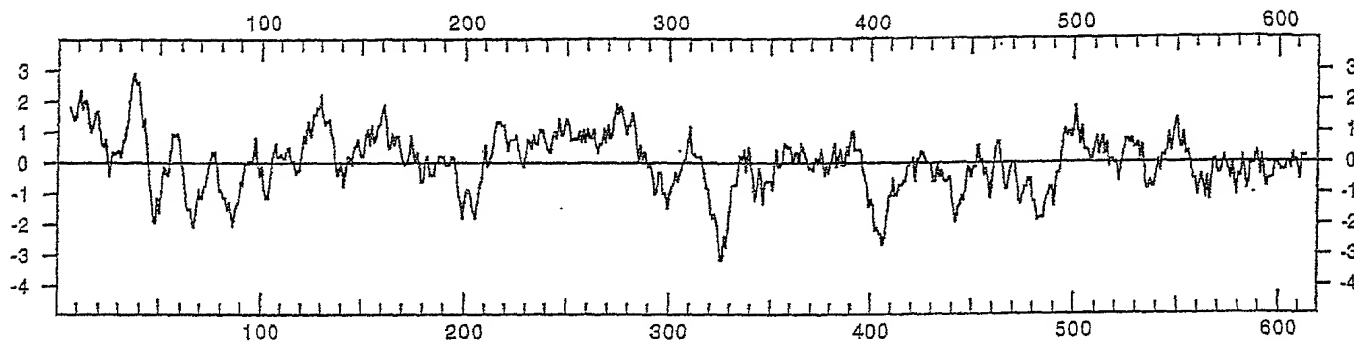


FIGURE 35 A

Protein sequence 619 a.a. MLLSWLTVLGAG ... LYDQIMLGEIKL

619 Amino Acids MW : 70066 Dalton

		n	n(%)	MW	MW(%)
A ala	alanine	33	5.3	2344	3.3
C cyst	cysteine	14	2.3	1442	2.1
D asp	aspartic acid	34	5.5	3910	5.6
E glu	glutamic acid	31	5.0	4000	5.7
F phe	phenylalanine	34	5.5	5000	7.1
G gly	glycine	44	7.1	2508	3.6
H his	histidine	13	2.1	1781	2.5
I ile	isoleucine	37	6.0	4184	6.0
K lys	lysine	48	7.8	6148	8.8
L leu	leucine	75	12.1	8481	12.1
M met	methionine	11	1.8	1441	2.1
N asn	asparagine	21	3.4	2394	3.4
P pro	proline	21	3.4	2038	2.9
Q gln	glutamine	18	2.9	2305	3.3
R arg	arginine	27	4.4	4214	6.0
S ser	serine	40	6.5	3481	5.0
T thr	threonine	30	4.8	3031	4.3
V val	valine	51	8.2	5052	7.2
W trp	tryptophan	11	1.8	2046	2.9
X ukw	unknown	-	-	-	-
Y tyr	tyrosine	26	4.2	4239	6.1
Z ---	STOP	-	-	-	-

FIGURE 35 B

1sFATP6 full length.protein

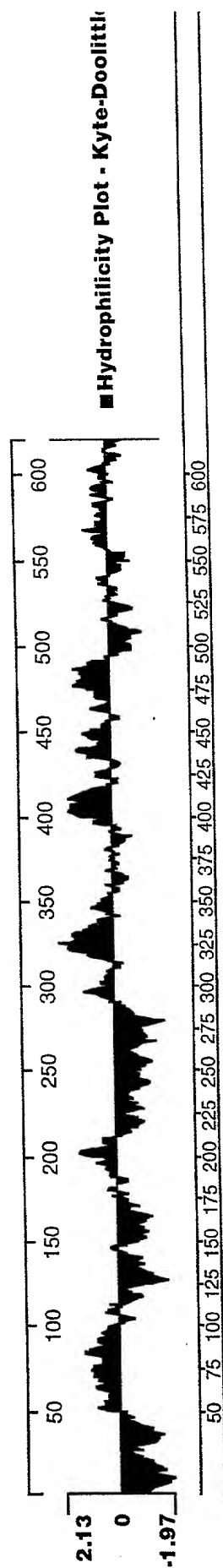


Figure 35C

1	M R A P - - G A G A S V S S A L W L G L P W T W S A A A A G V V G S G G W R F I R I V C K T A R R D L E G L	hsFATP1pep
1	L - - - - - F S K - V L K P W T Q V G S L I F L L G S G G W R I R V P I K T I R R D I E G G	hsFATP4pep
1	L L S W L T V L G G M V H P Q K L P Y F D D - - - - - F V K - - - - -	hsFATP6pep
59	S A R R V E L E L R R H Q R A G H I R I R Q A V Q O O P E R L A V D A G G E C U T E A O L D A S N A V A N	hsFATP1pep
46	L V L L K K A K A V R Q C L Q R R T V E I L R A T R R H P D T A I F G G D T H I T R Q L D E S S S V A N	hsFATP4pep
38	- V L L I I R L K Y E K R G L V R L D K L L H A K R Q E R P F I A Y G - - D I Y T Y Q D V D K R S R V A H	hsFATP6pep
119	- L F R Q L G F F P G D V A E L E G R E E V G P L G L A K A G M E A V L V N L R E P L A F C L G T S G A K	hsFATP1pep
106	- Q A R G L S G D V A I R M E A R N E A V G L W G M A C E G V E A I N T N I R D A I L H C E T A S R A H	hsFATP4pep
95	V E R N H S S K K G D T V A L L S N E E D F V H V F P L A L L G C V V F F N T N I R S N S I N G I R A C P R	hsFATP6pep
178	A I I E G G A V A A D V S G H E G K S E I K P G S G D L G E E I L D H L D D E E A S T A P L A Q I S	hsFATP1pep
165	A D V E G S E A S I C H A S L D P S E L C S G S W E G A P E S E H L D E E A D A K - H L P S C L D	hsFATP4pep
155	A D V I G A D L L G T E E I L P S E N I S V W G M K S V R Q G I S - - - L K E K S T S E D E S V R S H H	hsFATP6pep
238	- - - M D R R E E V T S G I T G L P C A R V V H S P E R A A F G H H Y R M Q A E V L D C I F L W H S	hsFATP1pep
224	- - - F T K R E Y E T S G T T G L P C A I V H E R V E R M A L V Y Y G E R R P N D A D C L P V H S	hsFATP4pep
211	V V S L L K S T C L T F T S L T G L P C A V I S Q L Q V L G S - - - L W E G C T H D V V I T P E V H S	hsFATP6pep
296	G N I I G V E G Q C H I Y L T V V R R G C F S A E R E W D D C P K Y N C T V V O V L G E I C R Y L L K O E V R E A E R R	hsFATP1pep
282	G N I V G I G C C H L H G M T V V I R K K P S A S T F W D D C K Y N C T I V G V L G E L C H A L N Q R P R E A E N Q	hsFATP4pep
270	A A L L G I L S G E V E L G A M C V L K K P S A S Q R S D C K Y V D V I V F O V D G E L C R Y L C R G S K R E G K D	hsFATP6pep
356	H R V R L A V G N G L R P A W E E F T E R R G V R Q I G E E V G A T E C A C S I A N M D G K V G S C G F N R L P H	hsFATP1pep
342	H O R M A L G N G L Q S I W T N F S S E H I P Q V A E E V G A T E C A C S L G M F D S Q V G A G G E N S R I S F	hsFATP4pep
330	H K V R L A I G N G I R S D V R E F L D R F G N I K C E L V A T E S S I S F M N Y T R I G A I G R T N L F Y K L	hsFATP6pep
416	P I R D V K V N E D T M E R L D A G L G I P C Q A G E P G L L V G Q I N O O D E L R E F D G V S E S T S K -	hsFATP1pep
402	P I R L V R V N E D E M E L I R G P D G V C L P C Q P G E P G O L M G R T I Q D E L R R E D G Y L N Q G N N K -	hsFATP4pep
390	L S T F D I K Y D F Q K D E P M R N E G W C H V K K G E P G L I S R V N A N E - - - E F G V A G P Y K H T K D	hsFATP6pep
475	K I A H S V S K I G D S A Y L - S G D V L M D E L G V M Y E R D R S G D T E K W R G E N V S I T E V E G V I S R L L G	hsFATP1pep
461	K I A K D V E K K G S Q A Y L - S G D V L M D E L G V M Y E R D R T G D T F R W G E N V S I T E V E G T E R L L D	hsFATP4pep
447	K L L C D V E K K G D - V A L N T S G L I M Q D N F L V E W D R T G D T E R W G E N V A T T E V A D V I G M I D F	hsFATP6pep
534	Q T E A V Y G V A V S V E E K A G M A V A - D E H S L D P N A I D E L Q R V I A P Y A R P I E L R D L R Q V D	hsFATP1pep
520	M A D V A V A G M E V I P G T E Q R A G M A V A - S I P T G N C D L E R F A C V E R E D L L A R P I E L R D L R E L H	hsFATP4pep
506	I Q E A N Y G V A I S I G Y E E K A G M A S I I L K P N T S L D L E K V E Q V V T P L R A C E R E L R I Q E K M E	hsFATP6pep
574	T T G R K I K T R I Q R E G D D P R Q T S R A L E P L D L K O G H L P E N E A V T E L C S G A F A	hsFATP1pep
560	K T G T Y F Q K T E R K E G F D P A I V K D E T R Y L D A C G R Y V E L D Q A V S R I Q A G E E K L	hsFATP4pep
546	A T G C P K L L K H Q L V E D G E N R L K I S E E Y E M D N L K S Y L T R S L D Q E M L G E I K T	hsFATP6pep

Coration 'Decoration #1': Shade (with solid bright yellow) residues that match the Consensus exactly.

Figure 36

Figure 37

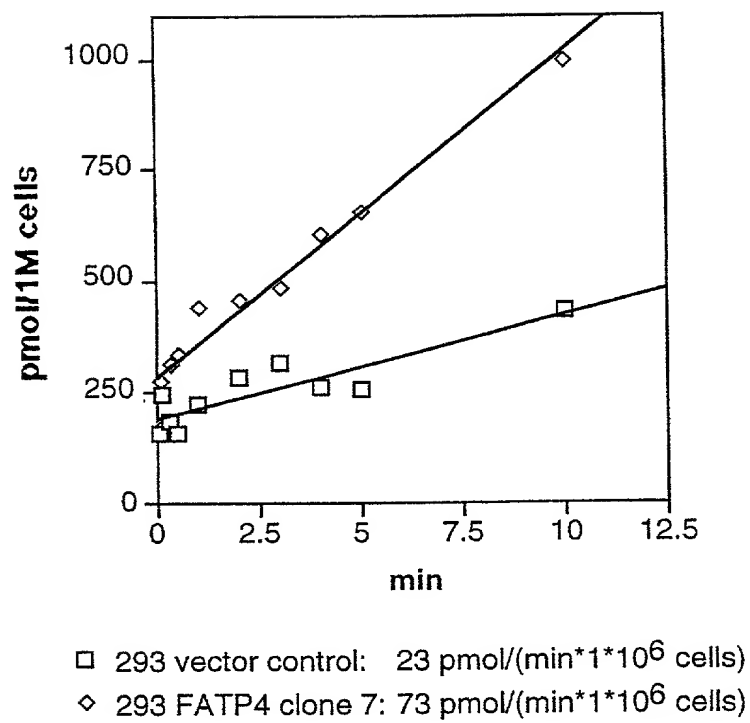


Fig. 38

hsFATP4 1
mmFATP4 1
hsFATP1 1

hsFATP4 46
mmFATP4 46
hsFATP1 48

hsFATP4 93
mmFATP4 93
hsFATP1 95

hsFATP4 140
mmFATP4 140
hsFATP1 142

hsFATP4 187
mmFATP4 187
hsFATP1 189

hsFATP4 233
mmFATP4 233
hsFATP1 236

hsFATP4 280
mmFATP4 280
hsFATP1 283

hsFATP4 327
mmFATP4 327
hsFATP1 330

hsFATP4 374
mmFATP4 374
hsFATP1 377

hsFATP4 421
mmFATP4 421
hsFATP1 424

hsFATP4 468
mmFATP4 468
hsFATP1 471

hsFATP4 515
mmFATP4 515
hsFATP1 518

hsFATP4 562
mmFATP4 562
hsFATP1 565

hsFATP4 609
mmFATP4 609
hsFATP1 612

156260-10550460

Fig. 40

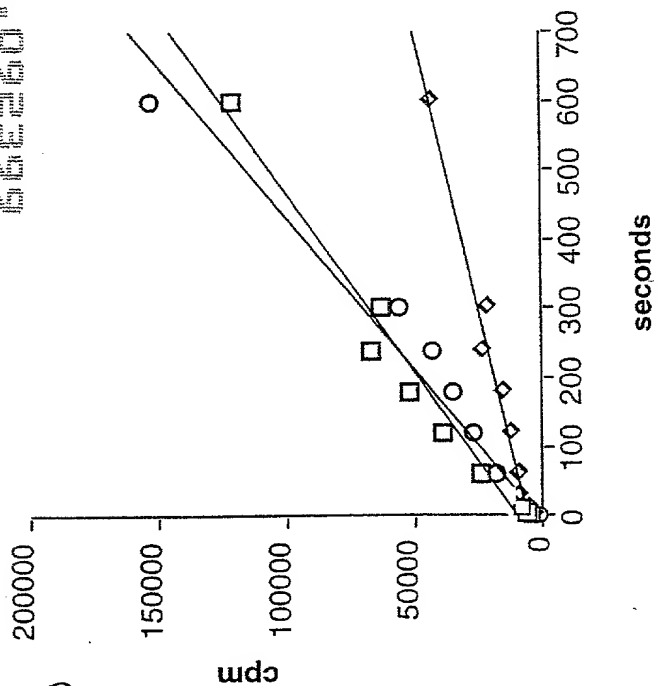


Fig. 41

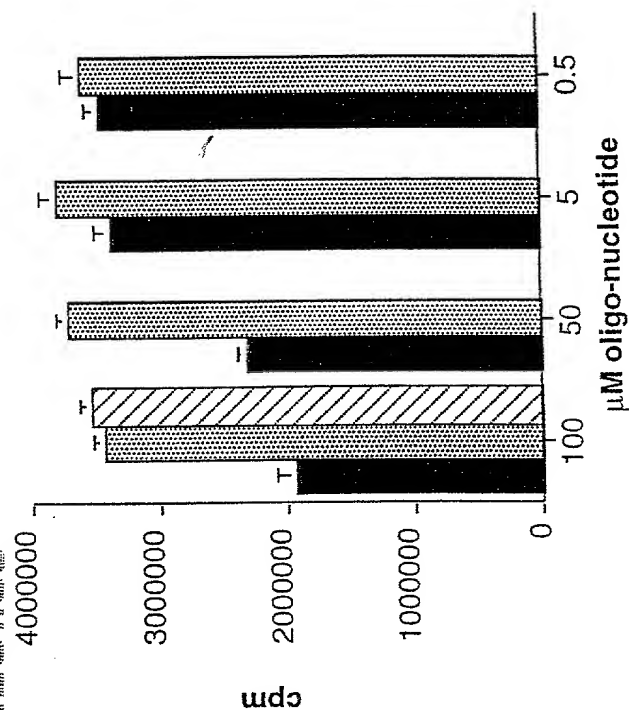
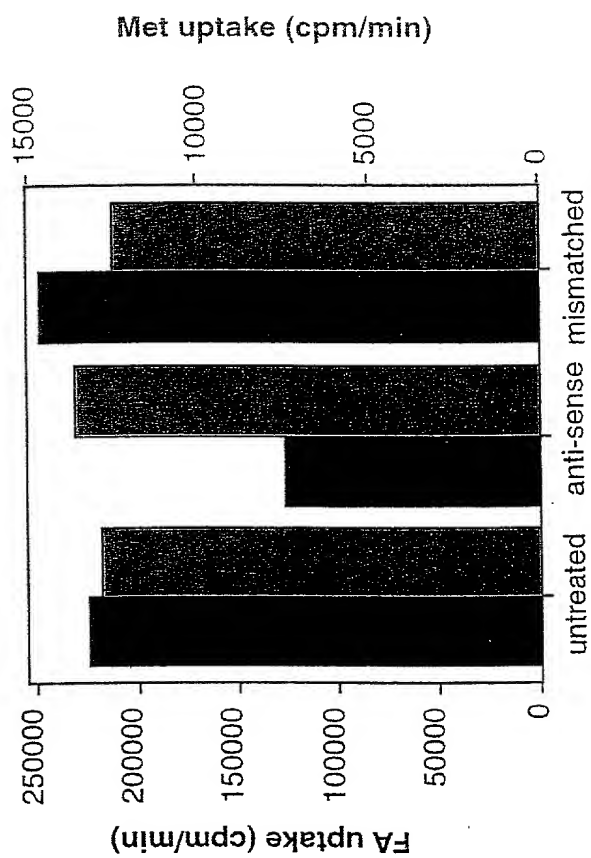


Fig. 42



mmFATP4 DNA sequence

ATGCTGCTTGGAGCCTCTCTGGTGGGGGCGCTACTGTTCTCCAAGCTAGTGCTGAAGCTGCCCTGGACCCAGGTGGGATT
CTCCCTGTTGCTCCTGTACTTGGGGTCTGGTGGCTGGCGTTTCATCCGGGTCTTCATCAAGACGGTCAGGAGAGATATCT
TTGGTGGCATGGTGCTCCTGAAGGTGAAGACCAAGGTGCGACGGTACCTTCAGGAGCGGAAGACGGTGCCCTGCTGTTT
GCTTCAATGGTACAGCGCCACCCGACAAAGACAGCCCTGATTTTCGAGGGGCACAGACACTCACTGGACCTTCCGCCAGCT
GGATGAGTACTCCAGTAGTGTGGCCAACTTCCTGCAGGCCCGGGGCTGGCCTCAGGCAATGTAGTTGCCCTCTTTATGG
AAAACCGCAATGAGTTTGTGGGTCTGTGGCTAGGCATGGCCAAGCTGGGCGTGGAGGCGGCTCTCATCAACACCAACCTT
AGGCGGGATGCCCCGCGCACTGTCTTGACACCTCAAAGGCACGAGCTCTCATCTTTGGCAGTGAGATGGCCTCAGCTAT
CTGTGAGATCCATGCTAGCCTGGAGCCCACTCAGCCTCTTCTGCTCTGGATCCTGGGAGCCAGCACAGTGCCCCGTCA
GCACAGAGCATCTGGACCCCTCTTCTGGAAGATGCCCCGAAGCAGCTGCCAGTCACCCAGACAAGGGTTTTACAGATAAG
CTCTTCTACATCTACACATCGGGCACCACGGGGCTACCCAAAGCTGCTATGACTGCCTCCCCCTCTACCACTCAAGCAGGA
TTCCCTGGTGTACTATGGATTCCGCATGCGGCCTGATGACATTGTCTATGACTGCCTCCCCCTCTACCACTCAAGCAGGA
AACATCGTGGGGATTGGCAGTGCTTACTCCACGGCATGACTGTGGTGATCCGGAAGAAGTTCTCAGCCTCCCCGGTTCTGG
GATGATTGTATCAAGTACAACCTGCACAGTGGTACAGTACATTGGCGAGCTCTGCCGCTACCTCCTGAACCAAGCCACCCG
TGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCAGTGGGCAACGGTCTCCGGCAGTCCATCTGGACCGACTTCTCCAGCC
GTTCCACATCCCCCAGGTGGCTGAGTTCTATGGGGCCACTGAATGCAACTGTAGCCTGGGCAACTTTGACAGCCGGGTG
GGGGCCTGTGGCTTCAATAGCCGCATCCTGTCTTTGTGTACCCTATCCGTTTGGTACGTGTCAATGAGGATACCATGGA
ACTGATCCGGGGACCCGATGGAGTCTGCATTCCCTGTCAACCAGGTGAGCCAGGCCAGCTGGTGGGTGCGCATCATCCAGC
AGGACCTCTGCGCCGTTTCGACGGGTACCTCAACCAGGTGCGCAACAACAAGAAGATTGCTAATGATGCTTCAAGAAG
GGGGACCAAGCCTACCTCACTGGTGACGTCCTGGTGATGGATGAGCTGGGTACCTGTACTTCCGAGATCGCACTGGGGA
CACGTTCCGCTGGAAGGGGAGAATGTATCTACCACTGAGGTGGAGGGCACACTCAGCCGCTGCTTCATATGGCAGATG
TGGCAGTTTATGGTGTGAGGTGCCAGGAACGAAGGCGGAGCAGGAATGGCTGCCGTTGCAAGTCCCATCAGCAACTGT
GACCTGGAGAGCTTTGCACAGACCTTGAAAAAGGAGCTGCCTCTGTATGCCCGCCCCATCTTCTGCGCTTCTTGCTGA
GCTGCACAAGACAGGGACCTTCAAGTTCAGAAAGACAGAGTTGCGGAAGGAGGGCTTTGACCCATCTGTTGTGAAAGACC
CGCTGTTCTATCTGGATGCTCGGAAGGGCTGCTACGTTGCACTGGACAGGAGGCCCTATACCCGCATCCAGGCAGGCGAG
GAGAAGCTGTGATTTCCCCCTACATCCCTCTGAGGGCCAGAAGATGCTGGATTGAGAGCCCTAGCGTCCACCCAGAGGG
TCCTGGGCAATGCCAGACCAAAGCTAGCAGGGCCCCGACCTCCGCCCCCTAGGTGCTGATCTCCCTCTCCCAAAGTCCA
AGTGAAGTCACTGCCGCTTCCCCGACCTCCAGAGGCTTTCTGTGAAAGTCTCATCCAAGCTGTGTCTTCTGTTCCAGGCG
TGGCCCCCTGGCCCCAGGGTTTCTGATAGGCTCCTTTAGGATGGTATCTTGGGTCCAGCGGGCCAGGGTGTGGGAGAGGAG
TCACTAAGATCCCTCCAATCAGAAGGGAGCTTACAAAGGAACCAAGGCAAGCCTGTAGACTCAGGAAGCTAAGTGGCCA
GAGACTATAGTGGCCAGTCACTCCATGTCCACAGAGGATCTTGGTCCAGAGCTGCCAAAGTGTACCTCTCCCTGCCTGC

ACCTCTGGGGAAAAGAGGACAGCATGTGGCCACTGGGCACCTGTCTCAAGAAGTCAGGATCACACACTCAGTCCTTGT
CTCCAGGTTCCCTTGTCTGTCTCGGGGAGGGAGGGACGAGTGTCTGTCTGCTCCTTCTGCTGTGAGTCTGTG
TTGCTTCTCATCTGCTCCTAGCCTGAGTGTGGGTGGAACAGGCATGAGGAGAGTGTGGCTCAGGGGCCAATAAACTCTGC
CTTGACTCCTCTTAAAAA

Figure 43A

mmFATP4 protein sequence

MLLGASLVGALLFSKLVKLPLWTVQVFSLLLLYLGS GGWRFFIRVFIKTVRRDIFGGMVLLKVKTKVRRYLQERKTVPLLF
ASMVQRHPDKTALIFEGTDTHWTFRLDEYSSSVANFLQARGLASGNVVALFMENRNEFVGLWLGMAKLGVEALINTNL
RRDALRHCLDTSKARALIFGSEMAIICEIHASLEPTLSLFCSGSWEPTVPVSTEHLDPILLEDAPKHLPSHPDKGFTDK
LFYIYTSGTTGLPKAAIVVHSRYRYMASLVVYGFMRPDDIVYDCLPLYHSSRKHRGDWQCLLHGTMVTVIRKFSASRFW
DDCIKYNCTVVQYIGELCRYLLNQPPREAESRHKVRMALGNLRSIWTDFSSRFHIPQVAEFYGATECNCSLGNFDSRV
GACGFNSRILSFVYPIRLVRVNETMELIRGPDGVCIPCQPGQPGQLVGRILQQDPLRRFDGYLNQGANNNKIANDVFKK
GDQAYLTGDLVMDLGYLYFRDRTGDTFRWKGENVSTTEVEGTLRLLHMDVAVYGVVPGTEGRAGMAAVASPI SNC
DLESFAQTLKKELPLYARPIFLRFLPELHKTGTFFKQKTELKKEGFDPSVVKDPLFYLDARKGCYVALDQEAYTRIQAGE
EKL

Figure 43B

hsFATP1 full lenght.DNA

10 20 30 40
TCGACCCACGGCGTCCGGGACCCCAAAGCAGAAGCCCGCA 40
CAGTAGGCACAGCGCACCCAAAGAAGGGTCCAGGAGTCTGC 80
AGAAACAGAAAGGTCCCCGGCCTCAGCCTCCTAGTCCCTG 120
CCTGCCTCCTGCCTGAGCTTCTGGGAGACTGAAGGCACGG 160
CTTGACGCTTCAGGATGCGGGCTCCGGGTGCGGGCGCGGC 200
210 220 230 240
CTCGGTGGTCTCGCTGGCGCTGTTGTGGCTGCTGGGGCTG 240
CCGTGGACCTGGAGCGCGGCAGCGGCGCTCGGCGTGTACG 280
TGGGCAGCGGGCGGCTGGCGCTTCTGCGCATCGTCTGCAA 320
GACCGCGAGGCGAGACCTCTTCGGTCTCTGTGTCTGATC 360
CGCGTGCGCCTGGAGCTGCGGCGGCACCAGCGTGCCGGCC 400
410 420 430 440
ACACCATCCCGCGCATCTTTCAGGCGGTAGTGCAGCGACA 440
GCCCCAGCGCCTGGCGCTGGTGGATGCCGGGACCGGCGAG 480
TGCTGGACCTTTGCGCAGCTGGACGCCTACTCCAATGCGG 520
TAGCCAAACCTTTCCGCCAGCTGGGCTTCGCGCCGGGCGA 560
CGTGGTGGCCATCTTCTGGAGGGCCGGCCGGAGTTTCGTG 600
610 620 630 640
GGGCTGTGGCTGGGCCTGGCCAAGGCGGGCATGGAGGCCG 640
CGCTGCTCAACGTGAACCTGCGGCGCGAGCCCCTGGCCTT 680
CTGCCTGGGACCTCGGGCGCTAAGGCCCTGATCTTTGGA 720
GGAGAAATGGTGGCGGCGGTGGCCGAAGTGAGCGGGCATC 760
TGGGGAAAAAGTTTGATCAAGTTCTGCTCTGGAGACTTGGG 800
810 820 830 840
GCCCCAGGGCATCTTGCCGGACACCCACCTCCTGGACCCG 840
CTGCTGAAGGAGGCCTCTACTGCCCCCTTGGCACAGATCC 880
CCAGCAAGGGCATGGACGATCGTCTTTTCTACATCTACAC 920
GTCGGGGACCACCGGGCTGCCCAAGGCTGCCATTGTCTGTG 960
CACAGCAGGTACTACCGCATGGCAGCCTTCGGCCACCACG 1000
1010 1020 1030 1040
CCTACCGCATGCAGGCGGCTGACGTGCTCTATGACTGCCT 1040
GCCCCGTGTAACCTCGGCAGGAAACATCATCGGCGTGGGG 1080
CAGTGTCTCATCTATGGGCTGACAGTCGTCTCCGCAAGA 1120
AATTCTCGGCCAGCCGCTTCTGGGACGACTGCATCAAGTA 1160
CAACTGCACGGTGGTTTCAGTACATCGGGGAGATCTGCCGC 1200

Fig. 44A

hsFATP1 full lenght.DNA

1210 1220 1230 1240
TACCTGCTGAAGCAGCCGGTGCGCGAGGCGGAGAGGCGAC 1240
ACCGCGTGCGCCTGGCGGTGGGGAACGGGCTGCGTCCTGC 1280
CATCTGGGAGGAGTTACGGAGCGCTTCGGCGTACGCCAA 1320
ATCGGGGAGTTCTACGGCGCCACCGAGTGCAACTGCAGCA 1360
TTGCCAACATGGACGGCAAGGTTCGGCTCCTGTGGTTTCAA 1400

1410 1420 1430 1440
CAGCCGCATCCTGCCCCACGTGTACCCCATCCGGCTGGTG 1440
AAGGTCAATGAGGACACAATGGAGCTGCTGCGGGATGCC 1480
AGGGCCTCTGCATCCCCTGCCAGGCCGGGAGCCTGGCCT 1520
CCTTGTTGGGTGAGATCAACCAACAGGACCCGCTGCGCCGC 1560
TTCGATGGCTATGTCAGCGAGAGCGCCACCAGCAAGAAGA 1600

1610 1620 1630 1640
TCGCCCACAGCGTCTTCAGCAAGGGCGACAGCGCCTACCT 1640
CTCAGGTGACGTGCTAGTGATGGATGAGCTGGGCTACATG 1680
TACTTCCGGGACCGTAGCGGGGACACCTTCCGCTGGCGAG 1720
GGGAGAACGTCTCCACCACCGAGGTGGAGGGCGTGCTGAG 1760
CCGCCTGCTGGGCCAGACAGACGTGGCCGTCTATGGGGTG 1800

1810 1820 1830 1840
GCTGTTCCAGGAGTGAGGGGTAAGGCAGGGATGGCGGCCG 1840
TCGCAGACCCCCACAGCCTGCTGGACCCCAACGCGATATA 1880
CCAGGAGCTGCAGAAGGTGCTGGCACCCCTATGCCCGGCC 1920
ATCTTCCTGCGCCTCCTGCCCCAGGTGGACACCACAGGCA 1960
CCTTCAAGATCCAGAAGACGAGGCTGCAGCGAGAGGGCTT 2000

2010 2020 2030 2040
TGACCCACGCCAGACCTCAGACCGGCTCTTCTTCCTGGAC 2040
CTGAAGCAGGGCCACTACCTGCCCTTAAATGAGGCAGTCT 2080
ACACTCGCATCTGCTCGGGCGCCTTCGCCCTCTGAAGCTG 2120
TTCCTCTACTGGCCACAACTCTGGGCCTGGTGGGAGAGG 2160
CCAGCTTGAGCCAGACAGCGCTGCCAGGGGTGGCCGCCT 2200

2210 2220 2230 2240
AGTACACACCCACCTGGCCGAGCTGTACCTGGCACGGCCC 2240
ATCCTGGACTGAGAACTGGAACCTCAGAGGAACCCGTGC 2280
CTCTCTGCTGCCTTGGTGCCCTGTGTCTGCCTCCTCTCC 2320
CTGCTTTTCAGCCTCTGTCTCCTTCCATCCCTGTCCCTGT 2360
CTGGCCTTAACCTCTTCCCTCTCTTTCTTTCTTTCTTTCT 2400

2410 2420 2430 2440
TTCTTTTTTTTTAAGATAGAGTCTCACTCTGCTGCCCGGG 2440
CTAGAGTGCACTGGTGGGATCTCGGCTCACTGCAACCTCT 2480
GCCTCCTGGGGTTCAAGTGATCCTCCCACCTCAGCCTCCT 2520
GAGTAGCTGGGATTACAGGCACCCGCCACCACGTCCAGCT 2560
AATTTTATATTTTATAGTAGAGACGGGGTTTACCATGTT 2600

Fig. 44B

00405504-092260

hsFATP1 full lenght.DNA

```

      2610      2620      2630      2640
      | | | | | | | | | | | | | | | | | |
GGTCAGGCTGGTCTTGAACCTCTGACCTCAGGTGATCCGC 2640
TGGCCTCGGCCTCCCAGAGTGCTGGGATTATAGGCGTGAG 2680
CCTGTGGCCCGGCCTTTCTTTTTCTCTCCTCTCCTGCC 2720
GAGAGTGGAACACACGTGTCCTGGGAGCTGCATCTTGTGT 2760
AGGGTCCAGCTGCTTTTGGGGACTGCAGGAATCATCTCCC 2800

      2810      2820      2830      2840
      | | | | | | | | | | | | | | | | | |
CTGGGCCCTGGACTCGGACTGGGGCCTCCCCACCTCCCTC 2840
TCGGCTGTGCCTTACGGAGCCCAATCCAGGCCTCCTGTG 2880
GCTGTTGGGTTCCAGATGCTGCAGCTCCATGTGACTTCCA 2920
AGCAGGCCCTCCGCCCTCCCTGCTGAATGGAGGAGCCGGG 2960
GGTCCCCCAGGCCAACTGGAAAATCTCCCAGGCTAGGCCA 3000

      3010      3020      3030      3040
      | | | | | | | | | | | | | | | | | |
ATTGCCTTTTGCACCTTCCCCGTTCTGTACATTTCCCCA 3040
GCCCCACCTTCCCCTCCTGATGCCCTGAAAGCTTCCGGAA 3080
TTGACTGTGACCACTTGGATGTCACCACTGTCAGCCCCTG 3120
CCTTGATGTCCCCATTTAGCCATCTCCATGGAGCTCCTGC 3160
TGGAGGGCCCTGAACCTGCACTGCGTGGCTGCCCAGCCA 3200

      3210      3220      3230      3240
      | | | | | | | | | | | | | | | | | |
GCTGCCTCCTGTCTTGGGAGGAGGCCTCCTGGGTGTCCTC 3240
ATCTGGTGTGTCTACTGGAGGGTCCCACAGGAGAGGCAGC 3280
AGAGGGGTGAGGGGAGGTCTCCTGCCGGGGGTGGCCTCT 3320
CAAGCCTCAGGGGTTCTAGCCTGTTGAATATACCCACCT 3360
GGTGGGTGGCCCTCCGATGTCCCCACTGATGGCTCTGAC 3400

      3410      3420      3430      3440
      | | | | | | | | | | | | | | | | | |
ACCGTGTTGGTGGCGATGTCCCAGACAATCCCACCAGGAC 3440
GGCCCAGACATCCCTACTGGCTTCGCTGGTGGCTCATCTC 3480
GAACATCCACGCCAGCCTTTCTGGGGCCGGCCACCCAGGC 3520
CGCCTGTCCGTCTGTCTCCCTCCAGCAGCACCCCTTGGC 3560
CCCTGGAGTGGTGGGGCCATGGCAAGAGACACCGTGGCGT 3600

      3610      3620      3630      3640
      | | | | | | | | | | | | | | | | | |
CTCATGTGAACCTTTCTGGGCACTGTGGTTTTATTTCTTA 3640
ATTGATTTAAGAAATAAACCTGAAGACCGTCTGGTGAAAA 3680
AAAAAAAAAAAAAA 3694

```

Fig. 44C

hsFATP1 full lenght.protein

10 20 30 40
MRAPGAGAASVSVSLALLWLLGLPWTWSAAAAALGVYVGSGG 40
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHQ RAGHTIPR 80
IFQAVVQRQPERLALVDAGTGECWTFAQLDAYSNVANLF 120
ROLGFAPGDVVAIFLEGRPEFVGLWLGLAKAGMEAALLNV 160
NLRREPLAFCLGTSGAKALIFGGEMVAAVA EVSGHLGKSL 200
210 220 230 240
IKFCSGDLGPEGILPDTHLLDPLLKEASTAPLAQIPSKGM 240
DDRLFYIYTS GTTGLPKAAIVVHSRYRMAAFGHHAYRMQ 280
AADVLYDCLPLYHSAGNIIGVGQCL IYGLTVVLRKKFSAS 320
RFWDDCIKYNCTVVQYIGEICRYLLKQPVREAERRHRVRL 360
AVGNGLRPAIWEETERFGVRQIGEFYGATECNC SIANMD 400
410 420 430 440
GKVGSCGFNSRILPHVYPIRLVKVNEDTMELLRDAQGLCI 440
PCQAGEPGLLVGQINQQDPLRRFDGYVSESATSKKIAHSV 480
FSKGDSAYLSGOVLVMDELGYMYFRDRSGDTFRWRGENVS 520
TTEVEGVLSRLLGQTDVAVYGVAVPGVEGKAGMAAVADPH 560
SLLOPNAIYQELQKVLAPYARPIFLRLLPQVD TTGTFKIQ 600
610 620 630 640
KTRLQREGFDPRQTSORLFFLDLKQGHYLP LNEAVYTRIC 640
SGAFAL. 647

Fig. 45

hsVLACS full lenght.DNA

10 20 30 40
 GGAATTCCAAAAAAAAAAAAATACGACTACACCTGCTCCGG 40
 AGCCCGCGGGCGGTACCTGCAGCGGAGGAGCTCTGTCTTCC 80
 CCTTCATCTCACGCGAGCCCGGCGTCCCGCCGCGTGCGCC 120
 CCGGCGCAGCCCGCCAGTCCGCGCGGAGCCCGCCAGTCG 160
 CCGCGCTGCACGCGCGGGGTGAACCCTCTGCCCTCGCTGG 200
 210 220 230 240
 GACAGAGGGCCCCGCAGCCGTCATGCTTTCCGCCATCTAC 240
 ACAGTCCTGGCGGGACTGCTGTTCTCCGCTCCTGGTGA 280
 ACCTCTGCTGCCCATACTTCTTCCAGGACATAGGCTACTT 320
 CTTGAAGGTGGCCGCGGTGGGCGGAGGGTGCGCAGCTAC 360
 GGGCAGCGGCGGCGGCGCGCACCATCCTGCGGGCGTTCC 400
 410 420 430 440
 TGGAGAAAGCGCGCCAGACGCCACACAAGCCTTTTCTGCT 440
 CTTCCGCGACGAGACTCTCACCTACGCGCAGGTGGACCGG 480
 CGCAGCAATCAAGTGGCCCCGGGCGCTGCACGACCACCTCG 520
 GCCTGCGCCAGGGAGACTGCGTGGGCGCTCCTTATGGGTAA 560
 CGAGCCGGCCTACGTGTGGCTGTGGCTGGGGCTGGTGAAG 600
 610 620 630 640
 CTGGGCTGTGCCATGGCGTGCCTCAATTACAACATCCGCG 640
 CGAAGTCCCTGCTGCACTGCTTCCAGTGCTGCGGGGCGAA 680
 GGTGCTGCTGGTGTGCGCCAGAACTACAAGCAGCTGTGCGAA 720
 GAGATACTGCCAAGCCTTAAAAAAGATGATGTGTCCATCT 760
 ATTATGTGAGCAGAACTTCTAACACAGATGGGATTGACTC 800
 810 820 830 840
 TTTCTGGACAAAGTGGATGAAGTATCAACTGAACCTATC 840
 CCAGAGTCATGGAGGTCTGAAGTCACTTTTCCACTCCTG 880
 CTTATACATTTATACTTCTGGAACCACAGGTCTTCCAAA 920
 AGCAGCCATGATCACTCATCAGCGCATATGGTATGGAAC 960
 GGCTCACTTTTGTAAAGCGGATTGAAGGCAGATGATGTCA 1000
 1010 1020 1030 1040
 TCTATATCACTCTGCCCTTTTACCACAGTGCTGCACTACT 1040
 GATTGGCATTACGGATGTATTGTGGCTGGTGCTACTCTT 1080
 GCCTTGCGGACTAAATTTTCAGCCAGCCAGTTTGGGATG 1120
 ACTGCAGAAAATACAACGTCACTGTCAATCAGTATATCGG 1160
 TGAAGTGCCTTCGGTATTTATGCAACTCACCACAGAAACCA 1200

Fig. 46 A

55250"40550460

hsVLACS full lenght.DNA

```

      1210      1220      1230      1240
      |-----|
AATGACCGTGATCATAAAGTGAGACTGGCACTGGGAAATG 1240
GCTTACGAGGAGATGTGTGGAGACAATTTGTCAAGAGATT 1280
TGGGGACATATGCATCTATGAGTTCTATGCTGCCACTGAA 1320
GGCAATATTGGATTTATGAATTATGCGAGAAAAGTTGGTG 1360
CTGTTGGAAGAGTAAACTACCTACAGAAAAAAATCATAAC 1400

      1410      1420      1430      1440
      |-----|
TTATGACCTGATTAAATATGATGTGGAGAAAGATGAACCT 1440
GTCCGAGATGAAAATGGATATTGCGTCAGAGTTCCCAAAG 1480
GTGAAGTTGGACTTCTGGTTTGCAAATCACACAACCTTAC 1520
ACCATTTAATGGCTATGCTGGAGCAAAGGCTCAGACAGAG 1560
AAGAAAAAACTGAGAGATGTCTTTAAGAAAGGAGACCTCT 1600

      1610      1620      1630      1640
      |-----|
ATTTCAACAGTGGAGATCTCTTAATGGTTGACCATGAAAA 1640
TTTCATCTATTTCCACGACAGAGTTGGAGATACATTCCGG 1680
TGGAAAGGGGAAAATGTGGCCACCACTGAAGTTGCTGATA 1720
CAGTTGGACTGGTTGATTTTGTCCAAGAAGTAAATGTTTA 1760
TGGAGTGCATGTGCCAGATCATGAGGGTCGCATTGGCATG 1800

      1810      1820      1830      1840
      |-----|
GCCTCCATCAAAATGAAAGAAAACCATGAATTTGATGGAA 1840
AGAAACTCTTTTCAGCACATTGCTGATTACCTACCTAGTTA 1880
TGCAAGGCCCGGTTTCTAAGAATACAGGACACCATTGAG 1920
ATCACTGGAACCTTTTAAACACCGCAAAATGACCCTGGTGG 1960
AGGAGGGCTTTAACCCCTGCTGTCATCAAAGATGCCTTGTA 2000

      2010      2020      2030      2040
      |-----|
TTTCTTGATGACACAGCAAAAATGTATGTGCCTATGACT 2040
GAGGACATCTATAATGCCATAAGTGCTAAAACCCCTGAAAC 2080
TCTGAATATTCCCAGGAGGATAACTCAACATTTCCAGAAA 2120
GAAACTGAATGGACAGCCACTTGATATAATCCAACTTTAA 2160
TTTGATTGAAGATTGTGAGGAAATTTGTAGGAAATTTGC 2200

      2210      2220      2230      2240
      |-----|
ATACCCGTAAAGGGGAGACTTTTTTAAATAACAGTTGAGTC 2240
TTTGCAAGTAAAAAGATTTAGAGATTATTATTTTTCAGTG 2280
TGCACCTACTGTTTGTATTTGCAAACTGAGCTTGTTGGAG 2320
GGAAGGCATTATTTTTTAAATACTTAGTAAATTAAATGA 2360
AC 2362

```

Fig. 4B

66250-10550-160

hsVLACS full lenght.protein

...

10 20 30 40
 MLSAIYTVLAGLLFLPLLVLNCCPYFFQDIGYFLKVA AVG 40
 RRVRSYGQRRPARTILRAFLEKARQTPHKPFLLFRDETLT 80
 YAQVDRRSNQVARALHDHLGLRQDCVALLMGNEPAYVWL 120
 WLGLVKLGCMACLNYNIRAKSLLHCFQCCGAKVLLVSPE 160
 LQAAVEEILPSLKKDDVSIYYVSRTSNTDGDIDSFLOKVDE 200
 210 220 230 240
 VSTEPESWRSEVTFSTPALYIYTS GTTGLPKAAMITHQ 240
 RIWYGTGLTFVSGLKADDVIYITLPFYHSAALLIGIHGCI 280
 VAGATLALRTKFSASQFWDDCRKYNVTVIQYIGELLRYLC 320
 NSPQKPNDRDHKVRALGNGLRGDVWRQFVKRFGDICIYE 360
 FYAATEGNIGFMNYARKVGAVGRVNYLQKKIITYDLIKYD 400
 410 420 430 440
 VEKDEPVRDENG YCVRVPKGEVGLLVCKITQLTPFNGYAG 440
 AKAQTEKKKL R DVFKKGDLYFNSGDLLMVDHENFIYFHDR 480
 VGDTRFWKGENVATTEVADTVGLVDFVQEVNVYGVHVPDH 520
 EGRIGMASIKMKNHEFDGKKLFQHIADYLP SYARPRFLR 560
 IQDTIEITGT FKHKMTLVEEGFNPAVIKDALYFLDDTAK 600
 610 620 630 640
 MYVPMTEDIYNAISAKTLKL. 621

Fig. 47

hsFATP3 partial.DNA

```

      10      20      30      40
      |      |      |      |
AAGTTCTCGGCTGGTCAGTTCTGGGAAGATTGCCAGCAGC 40
ACAGGGTGACGGTGTTCAGTACATTGGGGAGCTGTGCCG 80
ATACCTTGTCAACCAGCCCCGAGCAAGGCAGAACGTGGC 120
CATAAGGTCCGGCTGGCAGTGGGCAGCGGGCTGCGCCCAG 160
ATACCTGGGAGCGTTTTGTGCGGCGCTTCGGGCCCCCTGCA 200

      210      220      230      240
      |      |      |      |
GGTGCTGGAGACATATGGACTGACAGAGGGCAACGTGGCC 240
ACCATCAACTACACAGGACAGCGGGGCGCTGTGGGGCGTG 280
CTTCCTGGCTTTACAAGCATATCTTCCCCTTCTCCTTGAT 320
TCGCTATGATGTCACCACAGGAGAGCCAATTCGGGACCCC 360
CAGGGGCACTGTATGGCCACATCTCCAGGTGAGCCAGGGC 400

      410      420      430      440
      |      |      |      |
TGCTGGTGGCCCCGGTAAGCCAGCAGTCCCCATTCTGGG 440
CTATGCTGGCGGGCCAGAGCTGGCCCAGGGGAAGTTGCTA 480
AAGGATGTCTTCCGGCCTGGGGATGTTTTCTTCAAACTG 520
GGGACCTGCTGGTCTGCGATGACCAAGGTTTTCTCGCTT 560
CCATGATCGTACTGGAGACACCTTCAGGTGGAAGGGGGAG 600

      610      620      630      640
      |      |      |      |
AATGTGGCCACAACCGAGGTGGCAGAGGTCTTCGAGGCCC 640
TAGATTTTCTTCAGGAGGTGAACGTCTATGGAGTCACTGT 680
GCCAGGGCATGAAGGCAGGGCTGGAATGGCAGCCCTAGTT 720
CTGCGTCCCCCCCCACGCTTTGGACCTTATGCAGCTCTACA 760
CCCACGTGTCTGAGAACTTGCCACCTTATGCCCCGCCCCG 800

      810      820      830      840
      |      |      |      |
ATTCTCAGGCTCCAGGAGTCTTTGGCCACCACAGAGACC 840
TTCAAACAGCAGAAAGTTCGGATGGCAAATGAGGGCTTCG 880
ACCCAGCACCCCTGTCTGACCCACTGTACGTTCTGGACCA 920
GGCTGTAGGTGCCTACCTGCCCCTCACAAGTCCCCGGTAC 960
AGCGCCCTCCTGGCAGGAAACCTTCGAATCTGAGAACTTC 1000

     1010      1020      1030      1040
     |      |      |      |
CACACCTGAGGCACCTGAGAGAGGAACTCTGTGGGGTGGG 1040
GGCCGTTGCAGGTGTACTGGGCTGTGAGGGATCTTTTCTA 1080
TACCAGAACTGCGGTCACTATTTTGTAATAAATGTGGCTG 1120
GAGCTGATCCAGCTGTCTTGACAAAAAAGGAGGAGGAGG 1160
AAAGGGCGGCCGC 1173

```

Fig. 48

hsFATP3partial.protein

10 20 30 40
 KFSAGQFWEDCQQHRVTVFQYIGELCRYLVNQPPSKAERG 40
 HKVRLAVGSGLRPDTWERFVRRFGPLQVLETYGLTEGNVA 80
 TINYTGQRGAVGRASWLYKHIFPFLIRYDVTTGEPIRD 120
 QGHCMATSPGEPGLLVAPVSQQSPFLGYAGGPPELAQ GKLL 160
 KDVFRPGDVFFNTGDLLVCDDQGFLRFHDRTGDTFRWKGE 200
 210 220 230 240
 NVATTEVAEVFEALDFLQEVNVYGVTVPGHEGRAGMAALV 240
 LRPPHALDLMQLYTHVSENLPYARPRFLRLQESLATTET 280
 FKQKVRMANEGFDPSTLSDPLYVLDAQVGAYLPLTTARY 320
 SALLAGNLRI. 331

Fig. 49

66260 "HSS0460

hsFATP4 full length

CGACCCACGCGTCCGGGCGGGCGGGGCCGGGCGGGCGGGCG 40
 GGGCTGGCGGGGCGGCCGGGCCATGCAGGGCGCAGAGCCG 80
 GCTAAACCCTGCTGAGACCCGGCTCCGTGCGTCCAGGGGC 120
 GGCTAATGCCCTCACGCTGTCTACGCTGCTGCAACCGGG 160
 CCGCATCTGGACGGGGCGCCGCGCGGGGAGCCGACGCCG 200

210 220 230 240
 GGCCACAATGCTGCTTGGAGCCTCTCTGGTGGGGGTGCTG 240
 CTGTTCTCCAAGCTGGTGCTGAAACTGCCCTGGACCCAGG 280
 TGGGATTCTCCCTGTTGTTCTCTACTTGGGATCTGGCGG 320
 CTGGCGCTTCATCCGGGTCTTCATCAAGACCATCAGGCGC 360
 GATATCTTTGGCGGCCTGGTCCTCCTGAAGGTGAAGGCAA 400

410 420 430 440
 AGGTGCGACAGTGCCTGCAGGAGCGGCGGACAGTGCCCAT 440
 TTTGTTTGCCTCTACCGTTTCGGCGCCACCCCGACAAGACG 480
 GCCCTGATCTTCGAGGGCACAGATACCCACTGGACCTTCC 520
 GCCAGCTGGATGAGTACTCAAGCAGTGTAGCCAACTTCCT 560
 GCAGGCCCGGGCCTGGCCTCGGGCGATGTGGCTGCCATC 600

610 620 630 640
 TTCATGGAGAACCGCAATGAGTTCGTGGGCCTATGGCTGG 640
 GCATGGCCAAGCTCGGTGTGGAGGCAGCCCTCATCAACAC 680
 CAACCTGCGGCGGGATGCTCTGCTCCACTGCCTCACCACC 720
 TCGCGCGCACGGGCCCTTGTCTTTGGCAGCGAAATGGCCT 760
 CAGCCATCTGTGAGGTCCATGCCAGCCTGGACCCCTCGCT 800

810 820 830 840
 CAGCCTCTTCTGCTCTGGCTCCTGGGAGCCCGGTGCGGTG 840
 CCTCCAAGCACAGAACACCTGGACCCTCTGCTGAAAGATG 880
 CTCCCAAGCACCTTCCCAGTTGCCCTGACAAGGGCTTCAC 920
 AGATAAACTGTTCTACATCTACACATCCGGCACCACAGGG 960
 CTGCCCCAAGGCCGCCATCGTGGTGCACAGCAGGTATTACC 1000

1010 1020 1030 1040
 GCATGGCTGCCCTGGTGTACTATGGATTCCGCATGCGGCC 1040
 CAACGACATCGTCTATGACTGCCTCCCCCTCTACCACTCA 1080
 GCAGGAAACATCGTGGGAATCGGCCAGTGCCTGCTGCATG 1120
 GCATGACGGTGGTGAATTCGGAAGAAGTTCTCAGCCTCCCG 1160
 GTTCTGGGACGATTGTATCAAGTACAACCTGCACGATTGTG 1200

Fig. 50A

040504.0326

hsFATP4 full length

1210 1220 1230 1240
 CAGTACATTGGTGAACGTGTGCCGCTACCTCCTGAACCAGC 1240
 CACCGCGGGAGGCAGAAAACCAGCACCAGGTTTCGCATGGC 1280
 ACTAGGCAATGGCCTCCGGCAGTCCATCTGGACCAACTTT 1320
 TCCAGCCGCTTCCACATACCCAGGTGGCTGAGTTCTACG 1360
 GGGCCACAGAGTGCAACTGTAGCCTGGGCAACTTCGACAG 1400

1410 1420 1430 1440
 CCAGGTGGGGGCTGTGGTTTCAATAGCCGCATCCTGTCC 1440
 TTCGTGTACCCCATCCGGTTGGTACGTGTCAACGAGGACA 1480
 CCATGGAGCTGATCCGGGGGCGGACGGCGTCTGCATTCC 1520
 CTGCCAGCCAGGTGAGCCGGGCCAGCTGGTGGGCCGCATC 1560
 ATCCAGAAAGACCCCTGCGCCGCTTCGATGGCTACCTCA 1600

1610 1620 1630 1640
 ACCAGGGCGCCAACAACAAGAAGATTGCCAAGGATGTCTT 1640
 CAAGAAGGGGGACCAGGCCTACCTTACTGGTGTGTGCTG 1680
 GTGATGGACGAGCTGGGCTACCTGTACTTCCGAGACCGCA 1720
 CTGGGGACACGTTCCGCTGGAAGGTGAGAACGTGTCCAC 1760
 CACCGAGGTGGAAGGCACACTCAGCCGCCTGCTGGACATG 1800

1810 1820 1830 1840
 GCTGACGTGGCCGTGTATGGTGTGAGGTGCCAGGAACCG 1840
 AGGGCCGGGCCGGAATGGCTGCTGTGGCCAGCCCCACTGG 1880
 CAACTGTGACCTGGAGCGCTTTGCTCAGGTCTTGGAGAAG 1920
 GAACTGCCCCCTGTATGCGCGCCCCATCTTCTGCGCCTCC 1960
 TGCCTGAGCTGCACAAAACAGGAACCTACAAGTTCCAGAA 2000

2010 2020 2030 2040
 GACAGAGCTACGGAAGGAGGGCTTTGACCCGGCTATTGTG 2040
 AAAGACCCGCTGTTCTATCTAGATGCCCAGAAGGGCCGCT 2080
 ACGTCCCGCTGGACCAAGAGGCCTACAGCCGCATCCAGGC 2120
 AGGCGAGGAGAAGCTGTGATTCCCCCATCCCTCTGAGGG 2160
 CCGGCGGATGCTGGATCCGGAGCCCCAGGTTCCGCCCCAG 2200

2210 2220 2230 2240
 AGCGGTCTTGGACAAGGCCAGACCAAAGCAAGCAGGGCCT 2240
 GGCACCTCCATCCTGAGGTGCTGCCCCCTCCATCCAAAAC 2280
 GCCAAGTGACTCATTGCCTTCCCAACCCTTCCAGAGGCTT 2320
 TCTGTGAAAGTCTCATGTCCAAGTTCCGTCTTCTGGGCTG 2360
 GGCAGGCCCTCTGGTTCAGGCTGAGACTGACGGGTTTT 2400

2410 2420 2430 2440
 CTCAGGATGATGTCTTGGGTGAGGGTAGGGAGAGGACAAG 2440
 GGGTCACCGAGCCCTTCCAGAGAGCAGGGAGCTTATAAA 2480
 TGGAACCAGAGCAGAAGTCCCCAGACTCAGGAAGTCAACA 2520
 GAGTGGGCAGGGACAGTGGTAGCATCCATCTGGTGGCCAA 2560
 AGAGAATCGTAGCCCCAGAGCTGCCCAAGTTCACTGGGCT 2600

Fig. 50B

0045504-00550460

SECRET

Fig. 50C

hsFATP4 full length. protein

10 20 30 40
 MLLGASLVGVLLFSKLVKLPWTQVGFSLFLYLGGGWR 40
 FIRVFIKTIRRDIFGGLVLLKVKAKVRQCLQERRTPILF 80
 ASTVRRHPDKTALIFEGTDTHWTFRQLDEYSSSVANFLQA 120
 RGLASGDVAAIFMENRNEFVGLWLGMAKLGVEAALINTNL 160
 RRDALLHCLTTSRARALVFGSEMASAICEVHASLDPSLSL 200
 210 220 230 240
 FCSGSWEPGA VPPSTEHLDP LLDAPKHL PSCPDKGFTDK 240
 LFYIYTSGTTGLPKAAIVVHSRYRMAALVYYGFRMRPND 280
 IVYDCLPLYHSAGNIVGIGQCLLHG MTTVIRKKFSASRFW 320
 DDCIKYNCTIVQYIGELCRYLLNQPPREAEHQHVRMALG 360
 NGLRQSIWTFNFSRFHIPQVAEFYGATECNC SLGNFDSQV 400
 410 420 430 440
 GACGFNSRILSFVYPIRLVRVNEDTMELIRGPDGVCIPCQ 440
 PGEPGQLVGRIIQKDPLRRFDGYLNQGANNKKIAKDVFKK 480
 GDOAYLTGDVLVMDLGYLYFRDRTGDTFRWKGENVSTTE 520
 VEGTLSRLLDMADVAVYGVEVPGTEGRAGMAAVASPTGNC 560
 DLERFAQVLEKELPLYARPIFLRLLPELHKTGT YKFQKTE 600
 610 620 630 640
 LRKEGFDPAIVKDPLFYLD A QKGRYVPLDQ EAYSRIQAGE 640
 EKL 643

Fig. 51

>hsFATP5(partial)

GTCGTTGGGATCCTCGGCTGCTTAGATCTCGGAGCCACCTGTGTTCTGGCCCCCAAG
TTCTCTACTTCCTGCTTCTGGGA
TGACTGTCGGCAGCATGGCGTGACAGTGATCCTGTATGTGGGCGAGCTCCTGCGATA
CTTGTGTAACATTCCCCAGCAAC
CAGAGGACCGGACACATACAGTCCGCCTGGCAATGGGCAATGGACTACGGGCTGAT
GTGTGGGGAGACCTTCCAGCAGCG
TTTCGGTCCTATTTTCGGATCTNNGGGAAGTCTTACGGGCTTCCACAGAAGGGCAACAT
GGGGCTTTAGTTCAAATATTGTT
GGGGGCGCTGCGGGGGCCCTGGGGGGCAAAGATGGAGCTTGCCTCCTCCGAATGCTGT
CCCCCTTTGAGCTGGTGCAGTTTCG
ACATGGAGGCGGCGGAGCCTGTGAGGGACAATCAGGGCTTCTGCATCCCTGTAGGG
CTAGGGGAGCCGGGGCTGCTGTTG
ACCAAGGTGGTAAGCCAGCAACCCTTCGTGGGCTACCGCGGCCCCCGAGAGCTGTC
GGAACGGAAGCTGGTGCGCAACGT
GCGGCAATCGGGCGACGTTTACTACAACACCGGGGACGTAAGTGGCCATGGACCGCG
AAGGCTTCCTCTACTTCCGCGACC
GACTCGGGGACACCTTCCGATGGAAGGGCGAGAACGTGTCCACGCACGAGGTGGAG
GGCGTGTTGTCGCAGGTGGACTTC
TTGCAACAGGTTAACGTGTATGGCGTGTCGTGCCAGGTTGTGAGGGTAAGGTGGGC
ATGGCTGCTGTGGCATTAGCCCC
CGGCCAGACTTTCGACGGGGAGAAAGTTGTACCAGCACGTTTCGCGCTTGGCTCCCTGC
CTACGCTACCCCCCATTTTCATCC
GCATCCAGGACGCCATGGAGGTCAACAGCACGTTCAAACCTGATGAAGACCCGGTTG
GTGCGTGAGGGCTTCAATGTGGGG
ATCGTGGTTGACCCTCTGTTTGTACTGGACAACCGGGCCCAGTCCTTCCGGCCCCCTG
ACGGCAGAAATGTACCAGGCTGT
GTGTGAGGGAAACCTGGAGGCTCTGATCACCTGGCCAACCCACTGGGGTAGGGATCA
AAGCCAGCCACCCCCACCCCAACA
CACTCGGTGTCCCTTTCATCCTGGGCCTGTGTGAATCCCAGCCTGGCCATACCCTCA
ACCTCAGTGGGCTGGAAATGACA
GTGGGCCCTGTAGCAGTGGCAGAATAAACTCAGMTGYGTTCACAGAAA

Fig. 52

hsFATP5partial.protein

10 20 30 40
VVGILGCLDLGATCVLAPKFSTSCFWDDCRQHGVTVILYV 40
GELLRYLCNIPQQPEDRTHTVRLAMGNGLRADVWGDLPA 80
FRSYFGSXEVLRASLEGQHGALVQILLGALRGPGGKDGAC 120
LLRMLSPFELVQFDMEAAEPVRDNQGFCIPVGLGEPGLLL 160
TKVVSQQPFVGYRGPRELSEKLVNRNVRQSGDVYYNTGDV 200
210 220 230 240
LAMDREGFLYFRDRLGDTFRWKGENVSTHEVEGVLSQVDF 240
LQQVNVYGYCVPGCEGKVGMAAVALAPGQTFDGEKLYQHV 280
RAWLPAYATPHFIRIQDAMEVTSTFKLMKTRLVREGFNVG 320
IVVDPLFVLDNRAQSFRPLTAEMYQAVCEGTWRL 354

Fig. 53

65250-10550460

hsFATP6 full lenght.DNA

10 20 30 40
AACGGCAAGTAAGCGCAACGCAATTAATGTGAGTAGCTCA 40
CTCATTAGGCACCCCAGGCTTTACACTTTATGCTTCCGGG 80
CTCGTATGTTGTGTGGAATTGTGAGCGGATACCAATTTCA 120
CACAGGAACCAGCTATGACATGATTACGAATTTAATACGA 160
CTCACTATAGGGAATTTGGCCCTCGAGGCCAAGAATTCGG 200
210 220 230 240
CACGAGGGGTGCTGAGCCCTGCGCGGTTTCTGGTGCGTA 240
GAGACTGTAAATCGCTGCGCTTCTCAGTCATCATCATCCC 280
AGCTTTTCCCGGCTCGAATTCAGCCTCCAACCTCAAGCTCG 320
CGGGAAAGACTACCTGAGAGGAGAAAAGCTTCTGTCCCTG 360
GACCTTCTTCTGAGGGTGGAGTCCGAGGCTCCCTGCTTTC 400
410 420 430 440
CAGCCGCCCAGTGACCCAAGCTTAATCTTCAGCACCCTT 440
GGGGCGACCTTTTTCGGTGCAAACCTACGATTCTGTTTCTC 480
AGGATTCTCTCCCAATCCCGCTTCGCCCCGGAAAAGCTGAC 520
AAGAACTTCAGGTGTAAGCCCTGAGTAGTGAGGATCTGCG 560
GTCTCCGTGGAGAGCTGTGCCTGGAAGAGAAGGACGCTGG 600
610 620 630 640
TGGGGGCTGAGATCAGAGCTGTCTTCTGGCCCAGTTGCCC 640
CCATGCTTCTGTCATGGCTAACAGTTCTAGGGGCTGGAAT 680
GGTCGTCTTGCACCTTCTTGACAGAACTCCTGTTCCCTTAC 720
TTTTGGGATGACTTCTGGTTCGTGTTGAAGGTGGTGCTCA 760
TTATAATTCCGCTGAAGAAGTATGAAAAGAGAGGGGAGCT 800
810 820 830 840
GGTGACTGTGCTGGATAAATTCTTGAGTCATGCCAAAAGA 840
CAACCTCGGAAACCTTTTCATCATCTATGAGGGAGACATCT 880
ACACCTATCAGGATGTAGACAAAAGGAGCAGCAGAGTGGC 920
CCATGTCTTCTGAACCATTCCTCTCTGAAAAAGGGGGAC 960
ACGGTGGCTCTGCTGATGAGCAATGAGCCGGACTTCGTTT 1000
1010 1020 1030 1040
ACGTGTGGTTTCGGCCTCGCCAAGCTGGGCTGCGTGGTGGC 1040
CTTTCTCAACACCAACATTTCGCTCCAACCTCCCTCCTGAAT 1080
TGCATCCGCGCCTGTGGGCCCAGAGCCCTAGTGGTGGGCG 1120
CAGATTTGCTTGGAACGGTAGAAGAAATCCTTCCAAGCCT 1160
CTCAGAAAATATCAGTGTTTGGGGGATGAAAGATTCTGTT 1200

Fig. 54A

hsFATP6 full lenght.DNA

1210 1220 1230 1240
 CCACAAGGTGTAATTTCACTCAAAGAAAACTGAGCACCT 1240
 CACCTGATGAGCCCGTGCCACGCAGCCACCATGTTGTCTC 1280
 ACTCCTCAAGTCTACTTGTCTTTACATTTTTACCTCTGGA 1320
 ACAACAGGTCTACCAAAAGCAGCTGTGATTAGTCAGCTGC 1360
 AGGTTTTAAGGGGTTCTGCTGTCCTGTGGGCTTTTGTTG 1400

1410 1420 1430 1440
 TACTGCTCATGACATTGTTTATATAACCCTTCCTCTGTAT 1440
 CATAGTTCAGCAGCTATCCTGGGAATTTCTGGATGTGTTG 1480
 AGTTGGGTGCCACTTGTGTGTTAAAGAAGAAATTTTCAGC 1520
 AAGCCAGTTTTGGAGTGACTGCAAGAAGTATGATGTGACT 1560
 GTGTTTCAGTATATTGGAGAAGTTTGTGCTACCTTTGCA 1600

1610 1620 1630 1640
 AACAACTAAGAGAGAAGGAGAAAAGGATCATAAGGTGCG 1640
 TTTGGCAATTGGAAATGGCATACGGAGTGATGTATGGAGA 1680
 GAATTTTTAGACAGATTTGGAAATATAAAGGTGTGTGAAC 1720
 TTTATGCAGCTACCGAATCAAGCATATCTTTTCATGAAC 1760
 CACTGGGAGAATTGGAGCAATTGGGAGAACAAATTTGTTT 1800

1810 1820 1830 1840
 TACAACTTCTTTCCACTTTTGACTTAATAAAGTATGACT 1840
 TTCAGAAAGATGAACCCATGAGAAATGAGCAGGGTTGGTG 1880
 TATTCATGTGAAAAAAGGAGAACCTGGACTTCTATTTCT 1920
 CGAGTGAATGCAAAAAATCCCTTCTTTGGCTATGCTGGGC 1960
 CTTATAAGCACACAAAAGACAAATTGCTTTGTGATGTTT 2000

2010 2020 2030 2040
 TAAGAAGGGAGATGTTTACCTTAATACTGGAGACTTAATA 2040
 GTCCAGGATCAGGACAATTTCTTTATTTTGGGACCGTA 2080
 CTGGAGACACTTTTCAGATGGAAAGGAGAAAAATGTCGCAAC 2120
 CACTGAGGTTGCTGATGTTATTGGAATGTTGGATTTTATA 2160
 CAGGAAGCAAACGTCTATGGTGTGGCTATATCAGGTTATG 2200

2210 2220 2230 2240
 AAGGAAGAGCAGGAATGGCTTCTATTATTTTAAAACCAA 2240
 TACATCTTTAGATTTGGAAAAAGTTTATGAACAAGTTGTA 2280
 ACATTTCTACCAGCTTATGCTTGTCCACGATTTTAAAGAA 2320
 TTCAGGAAAAAATGGAAGCAACAGGAACATTCAAACATT 2360
 GAAGCATCAGTTGGTGGGAAGATGGATTTAATCCACTGAAA 2400

2410 2420 2430 2440
 ATTTCTGAACCACTTTACTTTCATGGATAACTTGAAAAAGT 2440
 CTTATGTTCTACTGACCAGGGAACCTTTATGATCAAATAAT 2480
 GTTAGGGGAAATAAACTTTAAGATTTTATATCTAGAAC 2520
 TTTTCATATGCTTTCTTAGGAAGAGTGAGAGGGGGGTATAT 2560
 GATTCTTTATGAAATGGGGAAAGGGAGCTAACATTAATTA 2600

Fig. 54B

hsFATP6 full lenght.DNA

```
      2610      2620      2630      2640
      | | | | | | | | | | | | | | | | | |
TGCATGTACTATATTTTCCTTAATATGAGAGATAATTTTTT 2640
AATTGCATAAGAATTTTAATTTCTTTTAATTGATATAAAC 2680
ATTAGTTGATTATTCTTTTTATCTATTTGGAGATTCAGTG 2720
CATAACTAAGTATTTTCCTTAATACTAAAGATTTTAAATA 2760
ATAAATAGTGGCTAGCGGTTTGGACAATCACTAAAAATGT 2800

      2810      2820      2830      2840
      | | | | | | | | | | | | | | | | | |
ACTTTCTAATAAGTAAAATTTCTAATTTTGAATAAAAAGAT 2840
TAAATTTTACTGAAAAAAAAAAAAAAAAAAAAAAAAAATTGGCG 2880
GCCGC 2885
```

Fig. 54C

hsFATP6 full lenght.protein

10 20 30 40
 MLLSWLTVLGAGMVVLHFLQKLLFPYFWDDFWVLKVYLI 40
 IIRLKKYEKRGELVTLDKFLSHAKRQPRKPFIIYEGDIY 80
 TYQDVDRSSRVAVHFLNHSSLKKGDTVALLMSNEPDFVH 120
 VWFGLAKLGCYVAFLENTNIRSNLLNCIRACGPRALVVGA 160
 DLLGTVEEILPSLSENISVWGMKDSVPQGVISLKEKLSTS 200
 210 220 230 240
 PDEPVPRSHHVVSLLKSTCLYIFTSGTTGLPKAAVISQLQ 240
 VLRGSAVLWAFGCTAHDIVYITLPLYHSSAAILGISGCV 280
 LGATCVLKKKFSASQFWSOCKKYDVTVFQYIGELCRYLCK 320
 QSKREGEKDHKVRLAIGNGIRSDVWREFLDRFGNIKVCEL 360
 YAATESSISFMNYTGRIGAIGRTNLFYKLLSTFDLIKYDF 400
 410 420 430 440
 QKDEPMRNEQGWCIVHKKGEPGLLISRVNAKNPFFGYAGP 440
 YKHTKDKLLCDVFKKGDVYLNTGDLIVQDQDNFLYFWDRT 480
 GDTFRWKGENVATTEVADVIGMLDFIQEANVYGVAISGYE 520
 GRAGMASIILKPNTSLDLEKVYEQVVTFLPAYACPRFLRI 560
 QEKMEATGTFKLLKHQLVEDGFNPLKISEPLYFMDNLKKS 600
 610 620 630 640
 YVLLTRELYDQIMLGEIKL. 620

Fig. 55

mFATP1 full length.DNA

10 20 30 40
 AAGTTCCTCACTCCAGACTTCTGCGAGAACCCGTGAGGAAG 40
 CAGCGAGAACCAGGGGGTTTGCAAGCCAGAGAAGGATGCGG 80
 ACTCCGGGAGCAGGAACAGCCTCTGTGGCCTCATTGGGGC 120
 TGCTTTGGCTTCTGGGACTTCCGTGGACCTGGAGCGCGGC 160
 GCGGCGGTTCGGTGTGTACGTGGGTAGCGGTGGCTGGCGA 200

210 220 230 240
 TTTCTGCGTATCGTCTGCAAGACGGCGAGGCGAGACCTCT 240
 TTGGCCTCTCTGTTCTGATCCGCGTGCGGCTAGAGCTACG 280
 ACGACACCGGCGAGCAGGAGACACGATCCACGCATCTTC 320
 CAGGCCGTGGCCCAGCGACAGCCGGAGCGCCTGGCGCTGG 360
 TAGATGCGAGTAGCGGTATCTGCTGGACCTTCGCACAGCT 400

410 420 430 440
 AGACACCTACTCCAATGCTGTGGCCAATCTGTTCTCCTCAG 440
 CTGGGCTTTGCGCCAGGCGATGTGGTGGCTGTGTTCTTG 480
 AAGGCCGGCCCCAGTTCTGTGGGACTGTGGCTGGGCCTGGC 520
 CAAGGCCGGTGTAGTGGCTTCGCTTCTCAATGTCAACCTG 560
 AGGCGGGAGCCCCCTTGCTTCTGCTTGGGCACATCAGCTG 600

610 620 630 640
 CCAAGGCCCTCATTTATGGCGGGGAGATGGCAGCGGCGGT 640
 GGCGGAGGTGAGTGAGCAGCTGGGGAAGAGCCTGCTCAAG 680
 TTCTGCTCTGGAGATCTGGGGCCTGAGAGCGTCCTGCCTG 720
 ACACGCAGCTTCTGGACCCCATGCTTGCTGAGGCGCCAC 760
 CACACCCCTGGCACAGGCCCCAGGCAAGGGCATGGATGAT 800

810 820 830 840
 CGGCTATTTTACATCTATACTTCTGGGACCACCGGACTTC 840
 CTAAGGCGGCCATTGTGGTGCACAGCAGGTACTACCGCAT 880
 CGCAGCCTTCGGCCACCATTCCTACAGCATGCGGGCCAAC 920
 GATGTGCTCTATGACTGCCTACCTCTCTACCACTCAGCAG 960
 GGAACATCATGGGCGTGGGACAGTGTATCATCTACGGGTT 1000

1010 1020 1030 1040
 AACGGTGGTACTGCGCAAGAAGTTCTCCGCCAGCCGCTTC 1040
 TGGGACGACTGTGTCAAATATAATTGCACGGTAGTGAGT 1080
 ACATCGGTGAAATATGCCGCTACCTGCTAAGGCAGCCGGT 1120
 TCGCGATGTAGAGCGGCGGCACCGCGTGCCTGGCCGTG 1160
 GGTAACGGACTGCGGCCAGCCATCTGGGAGGAGTTCACGC 1200

Fig. 56A

mFATP1 full length.DNA

```

      1210      1220      1230      1240
      |         |         |         |
AGGGTTTCGGTGTGCGACAGATTGGCGAGTTCTACGGCGC 1240
CACCGAATGCAACTGCAGCATTGCCAACATGGACGGCAAG 1280
GTCGGCTCCTGCGGCTTCAACAGCCGTATCCTCACGCATG 1320
TGTACCCCATCCGTCTGGTCAAGGTCAACGAGGACACGAT 1360
GGAGCCACTGAGGGACTCCCAAGGCCTCTGCATCCCGTGC 1400

      1410      1420      1430      1440
      |         |         |         |
CAGCCCGGGGAACCTGGGCTTCTCGTGGGCCAGATCAACC 1440
AGCAAGACCCTCTGCGGCGCTTCGATGGCTATGTTAGTGA 1480
CAGCGCCACCAACAAGAAGATTGCCACAGCGTGTTCGA 1520
AAGGGGGACAGCGCCTACCTTTTCAGGTGACGTGCTAGTGA 1560
TGGACGAGCTGGGGTACATGTACTTCCGTGACCGCAGCGG 1600

      1610      1620      1630      1640
      |         |         |         |
GGATACCTTCCGATGGCGCGGCGAGAACGTATCCACCACG 1640
GAGGTGGAAGCCGTGCTGAGCCGCCTGTTGGGCCAGACGG 1680
ACGTGGCTGTGTATGGAGTGGCTGTGCCAGGAGTGGAGGG 1720
GAAAAGCGGCATGGCGGCCATTGCAGACCCCCACAACCAG 1760
CTGGACCCCTAACTCAATGTACCAGGAATTGCAGAAGGTTC 1800

      1810      1820      1830      1840
      |         |         |         |
TTGCATCCTATGCCCAGCCCATCTTCCTGCGTCTTCTGCC 1840
CCAAGTGGATACAACAGGCACCTTCAAGATCCAGAAGACC 1880
CGACTACAGCGTGAAGGCTTTGACCCCCGCCAGACCTCAG 1920
ACCGGCTCTTCTTTCTAGACCTGAAACAGGGACGCTACCT 1960
ACCCCTGGATGAGAGAGTCCATGCCCCGCATCTGCGCAGGC 2000

      2010      2020      2030      2040
      |         |         |         |
GACTTCTCACTCTGAGCCTGGTGAAGTGGGATGGCCCTGGA 2040
CTTGTGAGACCAGGGAGCCGGACACCCCTGTTTCAGGTGTT 2080
TCTCCTGCCTGGCCACGTGGCCAGCAGCACCTGTGGGTGC 2120
AGGAAACTGGAACCTGAGTGGCCGGGTGTCCCTTTCTCTAC 2160
AACCACCATGCACACATCTAGCCTCTGCCTTGGTCTTTT 2200

      2210      2220      2230      2240
      |         |         |         |
TCTCCATCTCTTTCTCCGTGCCAGCAGGAGCCCCACAG 2240
ACACATTGGCTGCTGTGTCTGCAAGTGGGACCGGTGTCTA 2280
GGGGTCCATGCTGCAGGCTGTGACCCGCACTGGTGCCAC 2320
CTCCCTTCCCCATTGTGCCTTAGGTTCTCCACTGTGCGC 2360
CGGTGAAGCAAGTGGGGACCCACATAGCTGTTGTCCCTGC 2400

      2410      2420      2430      2440
      |         |         |         |
TGAGGGTTGGTAGCAAATGCACCCTCATGTCAGCTGGGAG 2440
ACACATGCAGTCTCCCACTGACCCCCAATCAACTGAAGAT 2480
ACTGTTTTGTATTATTGTTTTGAGATAGGGTCTCACTGTG 2520
GAGGCCAAGCTGGCCTCAGGCTCACCCTCTACTGCCTCC 2560
GGGCACCAGCCTGCAGTTTGATGACATGTATGCACTATTG 2600

```

Fig. 56B

040504 0360

1. The first step in the process is to identify the problem or issue that needs to be addressed. This involves gathering information and understanding the context of the problem.

2. Once the problem is identified, the next step is to define the objectives and goals of the project. This helps to clarify what needs to be achieved and provides a clear direction for the team.

3. The third step is to develop a plan or strategy to address the problem. This involves breaking down the problem into smaller, manageable tasks and determining the resources needed to complete each task.

4. The fourth step is to implement the plan. This involves putting the strategy into action and monitoring progress along the way. It is important to stay flexible and make adjustments as needed.

5. The final step is to evaluate the results of the project. This involves assessing whether the objectives were met and identifying any lessons learned for future projects.

Fig. 56C

mFATP1 full length.protein

10 20 30 40
MRTPGAGTASVASLGLLWLLGLPWTWSAAAAFGVYVGSGG 40
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHRRAGDTIPR 80
IFQAVAQRQPERLALVDASSGICWTFAQLDTYSNAVANLF 120
LQLGFAPGDVVAVFLEGRPEFVGLWLGLAKAGVVAALLNV 160
NLRREPLAFCLGTSAAKALIYGGEMAAAVAEVSEQLGKSL 200
210 220 230 240
LKFCSGDLGPESVLPDTQLLDPMLAEAPTTPLAQAPGKGM 240
DDRIFYIYTS GTTGLPKAAIVVHSRYRIA AFGHHSYSMR 280
ANDVLYDCLPLYHSAGNIMGVQCIIYGLTVVLRKKFSAS 320
RFWDDCVKYNCTVVQYIGEICRYLLRQPVRDVERRHRVRL 360
AVGNGLRPAIWEEFTQGFQVRQIGEFYGATECNC SIANMD 400
410 420 430 440
GKVGSCGFNSRILTHVYPIRLVKVNEDTMEPLRDSQGLCI 440
PCQPGEPGLLVGQINQQDPLRRFDGYVSDSATNKKIAHSV 480
FRKGDSAYLSGDVLVMDDELGYMYFRDRSGDTFRWRGENVS 520
TTEVEAVLSRLLGQTDVAVYGVAVPGVEGKSGMAAIADPH 560
NQLDPNSMYQELQKVLASYAQPIFLRLLPQVDTTGTFKIQ 600
610 620 630 640
KTRLQREGFDPRQTS DRLFFLDLKQGRYLPLDERVHARIC 640
AGDFSL. 647

Fig. 57

mVLACS(FATP2)full length.DNA

10 20 30 40
GACACAGTACTGCCGATGTTGGACAGAGGATCGCTTAACA 40
GAACGAAATCTCAAAACAAATTAACAGGACCCGGTTGCTT 80
GATTTCCCAAATCAGAAAAGGCTCGAAATGTCTAGAGGGG 120
CTGACTGATGCAGCGGTGACCCGGACTGGAGACAGTTGGA 160
CGCGATCATCTCTGGTGCTTTTGTTC AACCTTGAAACCTT 200

210 220 230 240
CGCCACAGGAGACTTGCTGAGCAGAGAAGCAAACGTGGA 240
GAAACAAAGAGAGATCTAGCGAAAAGCCTCTGGGACCAAG 280
GAGGGGAGGTGGGACTCTGGGTTGGCGGTGGCACCTGCTG 320
CCGGCTATTAATAATAGGGTCGCGATGCGTTTATAAGGTG 360
TTTGATTAACAAAGACTCTATGAGAGAAGAATAACTAGC 400

410 420 430 440
AACAGCCCCACGTCTGAGTCGTGCGCTCCGACCTTTTTTCA 440
ACGTGGGTTCTTTGGGCCGAGCGTCGTTTGCCGAGAACTA 480
GATCTCACCTGACCCCAGACGCTGAAAACAAGCGCTGTGG 520
CATCCTGGGCCACCCAAGCTGACAAGGGCGCGCCCCCTGA 560
GCACACGAGGTGCCCCACGAGGGGGAGGGACCCACAGCCG 600

610 620 630 640
TCCCGCCCGCACCGCGGTGTCCGCTGCGGGCACCTGCAGC 640
CGAGCCGCCACCCGAGTCGCAGCGCTCCGGCGGCCGAA 680
CCCGGTGCTCAGCTCGTCAGCACCTGCTCTGCTTCTCTCC 720
CGCCCCGCCGCCGCGCTGCACGCCTCGAGCGCTCCCTCGGC 760
CCCGGCGGGGACCGGGGACCCCGCAGCCACCGCCATGCTG 800

810 820 830 840
CCTGTGCTCTACACCGGCCTGGCGGGGCTGCTGCTGCTGC 840
CTCTGCTGCTCACCTGCTGCTGCCCCCTACCTCCTCCAGGA 880
CGTGCGGTTCTTCTGCAACTGGCCAACATGGCCCGGCAG 920
GTGCGCAGCTACCGGCAGCGGCGACCCGTGCGCACCATCC 960
TGCATGTCTTCTTGAGCAAGCGCGCAAGACCCCGCACAA 1000

1010 1020 1030 1040
GCCCTTCCTGCTGTTTTCGCGACGAGACGCTTACCTACGCC 1040
CAGGTAGACCGGCGCAGCAACCAAGTAGCGCGAGCGCTGC 1080
ATGATCACCTGGGCCTGCGGCAGGGGGATTGCGTGGCCCT 1120
CTTCATGGGCAATGAGCCGGCCTACGTGTGGCTCTGGCTG 1160
GGACTGCTCAAACCTGGGCTGTCCCATGGCGTGCCTCAACT 1200

Fig. 58A

00405504.0000

mVLACS(FATP2)full length.DNA

1210 1220 1230 1240
 ACAACATCCGTGCCAAGTCTCTGCTACACTGCTTTTCAGTG 1240
 CTGCGGGGCGAAGGTGCTGCTGGCCTCCCCAGAGCTACAC 1280
 GAAGCTGTGAGGAGGTTCTTCCAACCCTGAAAAAGGAGG 1320
 GCGTGTCCGTCTTCTACGTAAGCAGAACTTCTAACACTAA 1360
 TGGCCTGGACACAGTACTGGACAAAGTAGACGGGGTGTCTG 1400

1410 1420 1430 1440
 GCGGACCCCATCCCGGAGTCGTGGAGGTCTGAAGTCACGT 1440
 TCACCACACCCGCAGTCTACATATATACTTCGGGCACCAC 1480
 AGGTCTTCCAAAGGCTGCAACCATTAATCACCATCGCCTC 1520
 TGGTATGGGACCAGCCTTGCCCTGAGGTCCGGAATTAAGG 1560
 CTCATGACGTCACTACACCACCATGCCCCCTGTACCACAG 1600

1610 1620 1630 1640
 CGCGGCGCTCATGATTGGCCTCCACGGATGCATTGTGGTT 1640
 GGGGCTACATTTGCTTTGCGGAGCAAATTTTCAGCCAGCC 1680
 AGTTTTGGGACGACTGCAGGAAATACAACGCCACTGTCTAT 1720
 TCAGTACATCGGTGAACTGCTTCGGTACCTCTGCAACACG 1760
 CCCCAGAAACCAAATGACCGGGACCACAAAGTGGAAATAG 1800

1810 1820 1830 1840
 CACTAGGAAATGGCTTACGAGGAGATGTGTGGAGAGAGTT 1840
 CATCAAGAGATTTGGGGACATTACATTTATGAGTTCTAC 1880
 GCTTCCACTGAAGGCAACATTGGATTTATGAACTATCCAA 1920
 GAAAAATCGGAGCTGTTGGAAGAGAAAAATTACCTACAAAA 1960
 AAAAGTTGTAAGGCACGAGCTGATCAAGTATGACGTGGAG 2000

2010 2020 2030 2040
 AAGGATGAGCCTGTCCGTGATGCAAAATGGATATTGCATCA 2040
 AAGTCCCCAAAGGAGAGGTTGGACTCTTGATTTGCAAAAT 2080
 CACAGAGCTCACACCATTTTTTTGGCTATGCTGGAGGAAAG 2120
 ACCCAGACAGAGAAGAAAAAGCTCAGAGATGTTTTTAAGA 2160
 AAGGAGACGTCTACTTCAACAGTGGCGATCTCCTGATGAT 2200

2210 2220 2230 2240
 CGACCGTGAAAATTTTCATCTATTTTACGACAGAGTTGGA 2240
 GACACCTTCCGGTGGAAGGAGAGAATGTAGCTACCACGG 2280
 AAGTCGCTGACATTGTGGGACTGGTAGATTTTGTGGAAGA 2320
 AGTGAATGTTTACGGTGTGCCCCGTGCCAGGTCATGAAGGT 2360
 CGCATCGGGATGGCCTCGATCAAGATGAAAGAAAACACTACG 2400

2410 2420 2430 2440
 AGTTCAATGGAAAGAACTCTTTTCAGCACATCTCGGAGTA 2440
 CCTGCCCAGTTACTCGAGGCCTCGGTTCCCTGAGAATACAA 2480
 GATACCATTGAGATCACCGGGACTTTTAAACACCGCAAAG 2520
 TGACCCTGATGGAAGAGGGCTTTAACCCTCAGTCATCAA 2560
 AGATACCTTGATTTTCATGGATGACACAGAAAAACATAC 2600

Fig. 58B

THE **WORLD'S** **LARGEST** **BOOKSTORE**

Fig. 58C

mVLACS(FATP2)full length.prot

10 20 30 40
MLPVLYTGLAGLLLLPLLLTCCCPYLLQDVRFFLOLANMA 40
RQVRSYRQRRPVRTILHVFLEQARKTPHKPFLLFRDETLT 80
YAQVDRRSNQVARALHDHLGLRQGDCVALFMGNEPAYVWL 120
WLGLLKLGCMACLNYNIRAKSLLHCFQCCGAKVLLASPE 160
LHEAVEEVLP TLKKEGVSVFYVSRTSNTNGVDTVLDKVDG 200
210 220 230 240
VSADPIPESWRSEVTFITPAVYIYTS GTTGLPKAATINHH 240
RLWYGTSALRSGIKAHDVIYTTMPLYHSAALMIGLHGCI 280
VVGATFALRSKFSASQFWDDCRKYNATVIQYIGELLRYLC 320
NTPQKPNDRDHKVKIALGNGLRGDVWREFIKRFGDIHIYE 360
FYASTEIGNIGFMNYP RKIGAVGRENYLQKKVVRHEL IKYD 400
410 420 430 440
VEKDEPV RDANGYCIKVPKGEVGLLICKITELTPFFGYAG 440
GKTQTEKKKL RDVFKKGDVYFN SGDLLMIDRENFIYFHDR 480
VGDTFRWKGENVATTEVADIVGLVDFVEEVNVYGVVPVPGH 520
EGRIGMASIKMKENYEFNGKKLFQHISEYLP SYSRPRFLR 560
IQDTIEITGT FKHRKVTLMEEGFNPSVIKDTLYFMDDTEK 600
610 620 630 640
TYVPMTEDIYNAIIDKTLKL. 621

Fig. 59

1 10 20 30 40
GATCAGCTCTTCTATATCTACACGTGCGGCACCACGGGGC 40
TACCCAAAGCTGCCATTGTGGTGCACAGCAGGTATTACCG 80
AATGGCTGCCCTGGTGTACTATGGATTCCGCATGCGGCCT 120
GATGACATTGTCTATGACTGCCTCCCCCTCTACCACTCAG 160
CAGGAAACATTGTGGGGATTGGCCAGTGCCTACTCCACGG 200
210 220 230 240
CATGACTGTGGTGATCCGGAAGAAGTTTTTCAGCCTCCCGG 240
TTCTGGGATGACTGTATCAAGTACAAGTGCACAATTGTAC 280
AGTACATTGGTGAGCTTTGCCGCTACCTCCTGAACCAGCC 320
ACCCCGTGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCA 360
CTGGGCAACGGTCTCCGGCAGTCCATCTGGACCGACTTCT 400
410 420 430 440
CCAGCCGTTTCCACATTCCCAAGGTGGCCGAGTTCTACGG 440
GGCCACCGAGTGCAACTGTAGCTTGGGCAACTTTGACAGC 480
CAGGTGGGGGCTGTGGCTTCAATAGCCGCATCCTGTCCT 520
TTGTGTACCCCATCCGCTTGGTACGAGTCAATGAGGATAC 560
CATGGAAGTATCCGGGGACCCGATGGCGTCTGCATTCCC 600
610 620 630 640
TGTCACCAGGCCAGCCAGGCCAGCTGGTGGGTCGCATCA 640
TCCAGCAGGACCCCTACGCCGTTTTTGATGGCTACCTCAA 680
CCAGGGTGCCAACAACAAGAAGATTGCTAGTGATGTCTTC 720
AAGAAAGGGGACCAAGCCTACCTCACTGGTGACGTGCTGG 760
TGATGGATGAGCTGGGCTACCTGTACTTCCGAGACCGCAC 800
810 820 830 840
AGGGGACACGTTCCGCTGGAAAGGGGAGAATGTGTCTACC 840
ACTGAAGTGGAGGGCACACTCAGCCGCCTGCTTCAGATGG 880
CAGATGTGGCTGTTTATGGTGTGAGGTGCCAGGAGCTGA 920
GGGCCGAGCAGGAATGGCTGCTGTGGCAAGCCCCACTAGC 960
AACTGTGACCTGGAGAGCTTTGCACAGACCTTGAAAAAGG 1000
1010 1020 1030 1040
AGCTGCCCTGTACGCCCGCCCCATCTTCTCCGCTTCTT 1040
GCCTGAGCTGCACAAAACAGGAACCTTCAAGTTCCAGAAG 1080
ACAGAGTTGCGGAAGGAGGGCTTTGACCCGCTCTGTTGTGA 1120
AAGACCCACTCTTCTATTTGGATGCCCGGACAGGCTGCTA 1160
TGTTGCACTGGACCAAGAGGCCATATACCCGCATCCAGGCA 1200

Fig. 60A

[illegible]

Fig. 60B

mFATP4partial.DNA

10 20 30 40
 DQLFYIYTS GTTGLPKAAIVVHSRYRMAALVYYGFRMRP 40
 DDIVYDCLPLYHSAGNIVGIGQCVLHGMTVVIRKKFSASR 80
 FWDDCIKYNTIVQYIGELCRYLLNQPPREAESRHKVRMA 120
 LGNGLRQSIWTFSSRFHIPKVAEFYGATECNC SLGNFDS 160
 QVGACGFNSRILSFVYPIRLV RVNEDTMELIRGPDGVCIP 200
 210 220 230 240
 CQPGQPGQLVGR I IQQDPLRRFDGYLNQGANNKKIASDVF 240
 KKGDAQAYLTGDV LVMDELGYLYFRDRTGOTFRWKGENYST 280
 TEVEGTL SRLLQMA DVAVYGVEVPGAEGRAGMAAVASPTS 320
 NCDLESFAQTLKKELPLYARPIFLRFLPELHKTGTGFKFK 360
 TELRKEGFDP SVVKDPLFYLDARTGCYVALDQEAYTRIQA 400
 410 420 430 440
 GEEKL. 406

Fig. 61

mmFATP1 full length.DNA

1

10 20 30 40
 ATGCGGGCTCCTGGAGCAGGAACAGCCTCTGTGGCCTCAC 40
 TGGCGCTGCTTTGGTTTCTGGGACTTCCGTGGACCTGGAG 80
 CGCGGCGGCGGCGTTCTGTGTGTACGTGGGTGGCGGCGGC 120
 TGGCGCTTTCTGCGTATCGTCTGCAAGACGGCGAGGCGAG 160
 ACCTCTTTGGCCTCTCTGTTCTGATTCTGTTCGGCTAGA 200

210 220 230 240
 GCTGCGACGACACCGGCGAGCAGGAGACACGATCCCCTGC 240
 ATCTTCCAGGCTGTGGCCCGGCGACAACCAGAGCGCCTGG 280
 CACTGGTGGACGCCAGTAGTGGTATATGCTGGACCTTCGC 320
 ACAGCTGGACACCTACTCCAATGCTGTAGCCAACCTGTTC 360
 CGCCAGCTGGGCTTTGCACCAGGCGATGTGGTGGCTGTGT 400

410 420 430 440
 TCCTGGAGGGCGCGCCGGAGTTCTGTGGGACTGTGGCTGGG 440
 CCTGGCCAAGGCCGGTGTGGTGGCTGCTCTTCTCAATGTC 480
 AACCTGAGGCGGGAGCCCCCTGGCCTTCTGCCTGGGCACAT 520
 CAGCTGCCAAGGCCCTCATTTATGGCGGGGAGATGGCAGC 560
 GGCGGTGGCGGAGGTGAGCGAGCAGCTGGGGAAGAGCCTC 600

610 620 630 640
 CTCAAGTTCTGCTCTGGAGATCTGGGGCCTGAGAGCATCC 640
 TGCCTGACACGCAGCTCCTGGACCCCATGCTTGCTGAGGC 680
 GCCCACCACACCCCTGGCACAAGCCCCAGGCAAGGGCATG 720
 GATGATCGGCTGTTTTACATCTATACTTCTGGGACCACCG 760
 GGCTTCCTAAGGCTGCCATTGTGGTGCACAGCAGGTACTA 800

810 820 830 840
 CCGCATTGCTGCCTTTGGCCACCATTCTACAGCATGCGT 840
 GCCGCCGATGTGCTCTATGACTGCCTGCCACTCTACCACT 880
 CTGCAGGGAACATCATGGGTGTGGGGCAGTGCATCATCTA 920
 CGGGTTGACGGTGGTACTGCGCAAGAAGTTCTCCGCCAGC 960
 CGCTTCTGGGATGACTGTGTCAAGTACAATTGCACGGTAG 1000

1010 1020 1030 1040
 TGGATGACATAGGTGAAATCTGCCGCTACCTGCTGAGGCA 1040
 GCCGGTTCGCGACGTGGAGCAGCGACACCGCGTGCACCTG 1080
 GCCGTGGGTAATGGGCTGCGGCCAGCCATCTGGGAGGAGT 1120
 TCACGCAGCGCTTCGGTGTGCCACAGATCGGCGAGTTCTA 1160
 CGGCGCTACCGAGTGCAACTGCAGCATTGCCAACATGGAC 1200

Fig. 62A

002260-40550460

mmFATP1 full length.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
GGCAAGGTCGGCTCCTGCGGCTTCAACAGCCGTATCCTCA 1240
CGCATGTGTACCCCATCCGTCTGGTCAAGGTCAATGAGGA 1280
CACGATGGAGCCACTGCGGGACTCCGAGGGCCTCTGCATC 1320
CCGTGCCAGCCCGGGGAACCCGGCCTTCTCGTGGGCCAGA 1360
TCAACCAGCAGGACCCTCTGCGGCGTTTCGATGGTTATGT 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
TAGTGACAGTGCCACCAACAAGAAGATTGCCCACAGCGTT 1440
TTCCGAAAGGGCGATAGCGCCTACCTCTCAGGTGACGTGC 1480
TAGTGATGGACGAGCTGGGCTACATGTATTTCCGTGACCG 1520
CAGCGGGGACACCTTCCGCTGGCGCGGGGAGAACGTGTCC 1560
ACCACGGAGGTGGAAGCCGTGCTGAGCCGCCTACTGGGCC 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
AGACGGACGTGGCTGTGTATGGGGTGGCTGTGCCAGGAGT 1640
GGAGGGGAAAGCTGGCATGGCAGCCATCGCAGATCCCCAC 1680
AGCCAGTTGGACCCTAACTCAATGTACCAGGAATTACAGA 1720
AGGTTCTTGCATCCTATGCTCGGCCCATCTTCCTGCGTCT 1760
TCTGCCCCAGGTGGATACCACAGGCACCTTCAAGATCCAG 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
AAGACCCGGCTGCAGCGTGAAGGCTTTGACCCCCGTCAGA 1840
CCTCAGACAGGCTCTTCTTTCTAGACCTGAAGTCCGGCAC 1880
GAGGTATCTACCCCTGGATGAGAGAGTCCATGCCCGCATT 1920
TGCGCAGGCGACTTCTCACTCTGAGCCTGGAGAGTGGGCT 1960
GGGCCTGGACTCCTGAGACCTGGGAGCCTGACACCCCTCT 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
TCGGGTGCTTCTCCTGCCTGGCCACATGGACAGCAGCACC 2040
TGTGAGAGTAGGAAAATGGAACCTGAGTGGCTGGGACCCC 2080
TCTCCTACTTCCCCTATGCATCCATTTTGCCTCTGCCTT 2120
GATCTTTTTCTCCATCTCTTTTCTCCCTACCCAGCAGGAG 2160
CCCCACAAACACATGTTGGCTGCTGTGTCTGTCAGTTGGA 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
CCAGTGTCAGGGGTACAGGCTTCAGGCTGTGACCCACAC 2240
TGGTACCCACCTCCCTTTCTATTTTGCCTTAGGTTTCATC 2280
CACGGTTCCCCTGTGGAGCAAGTGGGGGCCCACATAGCTG 2320
CTGTCCCTGCTGAGGGTTGGTAGCAATCACACCCTCATGT 2360
CAGCTGGGAGACACGCGCAGTCTCCCACTGACCCCCAATC 2400

      2410      2420      2430      2440
      | | | | | | | | | | | | | | | |
AACTGAAAATATTGTTTTGACTACTTTTTGTTTTTTTGT 2440
TTTTTGTTTTTTTTTTTTTTTTCGAGACAGAGTTTCTCTGTA 2480
TAGCCCTGGCTGTCTTGGAACCTCACTTTGTAGACCAGGCT 2520
GGCCTCGAACTCAAAAATCCTCCTGACTCTGCCTCTGCTT 2560
CCCAAGTGCTGGGATTAAAGACGTGCGCCACCACCGCCTG 2600

```

Fig. 62B

66260"10550460

mmFATP1 full length.DNA

```

      2610      2620      2630      2640
      | | | | | | | | | | | | | | | | | |
GCTGTTTTGTATTTTGTGTTTGTGTTTGACGATAGGGTCTC 2640
ACTGTGGAGGCCAAGCTGGCCTCAGACTCCCCACCCCAT 2680
GCCTCTGGGCACCATTTCTATATTCTCAGACTGATGACAAT 2720
GCACTAGTGTCCCTAGGAGTCTTGAGTCTGCACTTTCCCC 2760
TCATAGCCTCAAGCTTCCAGAACTGACTCTGATCACTTGG 2800

      2810      2820      2830      2840
      | | | | | | | | | | | | | | | | | |
ATGTGGCTAGTGTTGGCTCTACCCACATGTGTCAATTCAG 2840
GGGTCCCCAGGCATAGTCTCTGGAAGCCCTCACCCGAAA 2880
AAGCTTGGAGAGACCCAGGAAGGTTGTTGTGTTCTCTTGG 2920
GCACCCCTGGTGGCAGTCCTGGGCATGCTTCCGCACTGT 2960
ACTGGTGCATATAGCCCAGACCTATGACATTTGAGGTCTA 3000

      3010      3020      3030      3040
      | | | | | | | | | | | | | | | | | |
CCCTTCTGGCTCCTGTGGTCCCCATTGAGATCCTTGGTGA 3040
CTCACCTCAGTCACCAAGCAGAGCCTCTGCCTGCCTTCAT 3080
CTTCAAGGTCATGAAGGATGTGGACAGAGCAGCTACAGGC 3120
TGCCAGCAGTCAACCACATGAGAGTGTTACTTCCTTGTTG 3160
GTTTTTAAAAAATAAATGTGCTGAGCCTCGAAAAAAAAAA 3200

      3210      3220      3230      3240
      | | | | | | | | | | | | | | | | | |
AAAAAAAAAAAAAAAAAA 3217

```

Fig. 62C

mmFATP1 full length.protein

10 20 30 40
MRAPGAGTASVASLALLWFLGLPWTWSAAAAFCVYVGGGG 40
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHRRAGDTIPC 80
IFQAVARRQPERLALVDASSGICWTFAQLDTYSNAVANLF 120
RQLGFAPGDVVAVFLEGRPEFVGLWLGLAKAGVVAALLNV 160
NLRREPLAFCLGTSAAKALIYGGEMAAVAEVSEQLGKSL 200
210 220 230 240
LKFCSGDLGPESILPDTQLLDPMLAEAPTTPLAQAPGKGM 240
DDRLFYIYTS GTTGLPKAAIVVHSRYRIA AFGHHSYSMR 280
AADVLYDCLPLYHSAGNIMGVGCVIYGLTVVLRKKFSAS 320
RFWDDCVKYNCTVDDIGEICRYLLRQPV RDVEQRHRVRL 360
AVGNGLRPAIWEEFTQRFQVPGIGEFYGATECNCSIANMD 400
410 420 430 440
GKVGSCGFNSRILTHVYPIRLVKVNEDTMEPLRDSEGLCI 440
PCQPGEPGLLVGQINQODPLRRFDGYVSDSATNKKIAHSV 480
FRKGDSAYLSGDVLVMDELGYMYFRDRSGDTFRWRGENVS 520
TTEVEAVLSRLLGOTDVAVYGVAVPGVEGKAGMAAIADPH 560
SQLDPNSMYQELQKVLASYARPIFLRLLPQVDTTGTFKIQ 600
610 620 630 640
KTRLQREGFDPRQTS DRLFFLDLKSGTRYLPLDERVHARI 640
CAGDFSL 647

Fig. 63

mmFATP2 full length.DNA

10 20 30 40
 GGGCGGAGGCCGAGCCAGTCGCCAGCTCCTGCTCTGCTC 40
 CTCTCCCGCCTGCCGCCGCGCTGCACGCCTCGAGCACTCC 80
 CTCGGCCCCGGCGGGGACCGGGGACCCCGCAGCTACCGCC 120
 ATGCTGCCAGTGCTCTACACCGGCCTGGCGGGGCTGCTGC 160
 TGCTGCCTCTGCTGCTCACCTGCTGCTGCCCCCTACCTCCT 200

210 220 230 240
 CCAAGATGTGCGGTACTTCCTGCGGCTGGCCAACATGGCC 240
 CGGCGGGTGCGCAGCTACCGGCAGCGGCGACCCGTGCGTA 280
 CCATCCTGCGGGCCTTCCTGGAACAAGCGCGCAAGACCCC 320
 ACACAAGCCCTTCCTGCTGTTCCGAGACGAGACGCTCACC 360
 TACGCCAGGTGGACCGGCGCAGCAACCAAGTGGCGCGGG 400

410 420 430 440
 CGCTGCACGATCAACTGGGCCTACGACAGGGGGATTGCGT 440
 AGCCCTCTTCATGGGCAATGAGCCGGCCTACGTGTGGATC 480
 TGGCTGGGACTGCTCAAACCTGGGCTGTCCCATGGCGTGCC 520
 TCAACTACAACATTTCGTGCCAAGTCTCTGCTGCACTGCTT 560
 TCAATGCTGCGGGGCGAAGGTGCTGCTGGCCTCCCCAGAT 600

610 620 630 640
 CTACAAGAAGCTGTGGAGGAGGTTCTTCCAACCCTGAAAA 640
 AGGATGCCGTGTCCGTCTTTTACGTAAGCAGAACTTCTAA 680
 CACAAATGGTGTGGACACAATACTGGACAAAGTAGACGGA 720
 GTGTGCGGCGGAACCCACCCCGAGTCGTGGAGGTCTGAAG 760
 TCACTTTTACCACGCCAGCAGTATACATTTATACTTCGGG 800

810 820 830 840
 AACCACAGGTCTTCCAAAAAGCGGAACCATCAATCATCAT 840
 CGCCTAAGGTATGGGACAAGCCTTGCTATGTGCGAGTGGGA 880
 ATCAGGCCCAAGGATGTCATCTATACCAACAATGCCCTG 920
 TTCCAACAGTGCAACGCTCAAGATCGGCCTTCACGGATGC 960
 ATCCTGGGTTGGGGCTACTTTAACCTTGGCGGGGCAAATT 1000

1010 1020 1030 1040
 CTCAAGCAAGCCAATTTTGGGAACGACTGGCAGGAAATAC 1040
 AACGTCAACGGTCATTCAGTACATTGGTGAAGTCTTCGG 1080
 TACCTGTGCAACACACCGCAGAAACCAATGACCGGGACC 1120
 ACAAGTGAAAAAAGCCCTGGGAAATGGCTTACGAGGAGA 1160
 TGTGTGGAGAGAGTTTCATCAAGAGATTTGGGGACATCCAC 1200

Fig. 64A

04550460

mmFATP2 full length.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
GTGTATGAGTTCTACGCATCCACTGAAGGCAACATTGGAT 1240
TTGTGAACTATCCAAGGAAAAATCGGTGCTGTCGGGAGAGC 1280
AAACTACCTACAAAGAAAAGTTGCAAGGTATGAGCTGATC 1320
AAGTATGACGTGGAGAAGGACGAGCCGGTCCGTGACGCAA 1360
ATGATATTGCATCAAAGTCCCCAAAGGTGAGGTTGGACT 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
CTTGTTTTGCAAAATCACACAGCTCACACCATTTATTGGC 1440
TATGCTGGAGGAAAGACCCAGACAGAGAAGAAAAAACTCA 1480
GAGATGTCTTTAAGAAAGGCGACATCTACTTCAACAGCGG 1520
AGACCTCCTGATGATCGACCGTGAGAACTTCGTCTACTTT 1560
CACGACAGGGTTGGAGATACTTTCCGGTGGAAAGGAGAGA 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
ACGTAGCTACCACAGAAGTCGCTGACATCGTGGGACTGGT 1640
AGATTTTGTGAAGAAGTGAATGTGTATGGCGTGCCTGTG 1680
CCAGGTCATGAGGGTCAATTTGGGATGGCCTCCCTCAAGA 1720
TCAAAGAAAACTACGAGTTCAATGGAAAGAACTCTTTCA 1760
ACACATCGCGGAGTACCTGCCAGTTACGCGAGGCCTCGG 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
TTCCTGAGGATACAAGATACCATTGAGATCACTGGGACTT 1840
TTAAACACCGCAAAGTGACCCTGATGGAAGAGGGCTTCAA 1880
TCCCACAGTCATCAAAGATACCTTGTATTTTCATGGATGAT 1920
GCAGAGAAAACATTTGTGCCCATGACTGAGAACATTTATA 1960
ATGCCATAATTGATAAAACTCTGAAGCTCTGAATATTCCC 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
TGGTGGTTTAGCTCATGACATTTCCAGAAAGAACTCGAT 2040
AGACCTCGCAGAGCCACTTCATACGTAGAATCCAACTTTA 2080
ACTTGATTGAAGACTATAAGGTGCGATTTTATTTTATAGGA 2120
AATTATTCATTAAGGATAGTTTTTTTTTTTTTTTTTAA 2160
TTACACCTGAACCTTTGCAAGTAAAAAGATTTAGAGACAA 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
TTATTTTTCAATGTGCACCTGCCATTTGTCCTTGCAAAC 2240
AAGCTTCTTGAGAGAGGGCCTTATTTTTTTAAAGACATA 2280
ATAAACTATATTAACATAAAAAAAAAAAAAAAAAAAAAA 2320
AAAAAAAAAAAAAAAAAAAA 2338

```

Fig. 64B

66260"40550460

SECRET

Fig. 65

mmFATP3 partial.DNA

```

      10      20      30      40
      |      |      |      |
GAAAGCTCTGAGAGCGGGTGCAGTCTGGCCTGGCGTCTCG 40
CGTACCTGGCCCGGGAGCAGCCGACACACACCTTCCTCAT 80
CCACGGCGCGCAGCGCTTTAGCTACGCGGAGGCTGAGCGC 120
GAGAGCAACCGGATTGCTCGCGCCTTTCTGCGCGCACGGG 160
GCTGGACCGGGGGCCGCCGAGGCTCGGGCAGGGGCAGCAC 200

      210      220      230      240
      |      |      |      |
TGAGGAAGGCGCACGCGTGGCGCCTCCGGCTGGAGATGCG 240
GCTGCTAGAGGGACGACCGCGCCCCCTCTGGCACCCGGGG 280
CGACCGTGGCGCTGCTCCTCCCAGCGGGCCCGGATTTCT 320
TTGGATTTGGTTCCGACTGGCCAAAGCTGGCCTGCGCACG 360
GCCTTTGTGCCACCGCTTTACGCCGAGGACCCCTGCTGC 400

      410      420      430      440
      |      |      |      |
ACTGCCTCCGCAGCTGCGGTGCGAGTGCCTCGTGCTGGC 440
CACAGAGTTCCTGGAGTCCCTGGAGCCGGACCTGCCGGCC 480
TTGAGAGCCATGGGGCTCCACCTATGGGCGACGGGCCCTG 520
AAACTAATGTAGCTGGAATCAGCAATTTGCTATCGGAAGC 560
AGCAGACCAAGTGGATGAGCCAGTGCCGGGGTACCTCTCT 600

      610      620      630      640
      |      |      |      |
GCCCCCAGAACATAATGGACACCTGCCTGTACATCTTCA 640
CCTCTGGCACTACTGGCCTGCCCAAGGCTGCTCGAATCAG 680
TCATCTGAAGGTTCTACAGTGCCAGGGATTCTACCATCTG 720
TGTGGAGTCCACCAGGAGGACGTGATCTACCTCGCACTCC 760
CACTGTACCACATGTCTGGCTCCCTTCTGGGCATTGTGGG 800

      810      820      830      840
      |      |      |      |
CTGCTTGGGCATTGGGGCCACCGTGGTGCTGAAACCCAAG 840
TTCTCAGCTAGCCAGTTCTGGGACGATTGCCAGAAACACA 880
GGGTGACAGTGTTCCAGTACATTGGGGAGTTGTGCCGATA 920
CCTCGTCAACCAGCCCCGAGCAAGGCAGAGTTTGACCAT 960
AAGGTGCGCTTGGCAGTGGGCAGTGGGTTGCGCCCAGACA 1000

      1010      1020      1030      1040
      |      |      |      |
CCTGGGAGCGTTTCTCGGGCGATTTGGACCTCTGCAGAT 1040
ACTGGAGACGTATGGCATGACAGAGGGCAACGTAGCTACG 1080
TTCAATTACACAGGACGGCAGGGTGCAGTGGGGCGAGCTT 1120
CCTGGCTTTACAAGCACATCTTCCCCTTCTCCTTGATTCT 1160
ATACGATGTCATGACAGGGGAGCCTATTCGGAATGCCAG 1200

```

Fig. 66A

09405504.09299

mmFATP3 partial.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
GGGCACTGCATGACCACATCTCCAGGTGAGCCAGGCCTAC 1240
TGGTGGCCCCAGTGAGCCAGCAGTCCCCCTTCCTGGGCTA 1280
TGCTGGGGCTCCGGAGCTGGCCAAGGACAAGCTGCTGAAG 1320
GATGTCTTCTGGTCTGGGGACGTTTTCTTCAATACTGGGG 1360
ACCTCTTGGTCTGTGATGAGCAAGGCTTTCTTCACTTCCA 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
CGATCGTACTGGAGACACCATCAGGTGGAAGGGAGAGAAT 1440
GTGGCCACAACCTGAAGTGGCTGAGGTCTTGGAGACCCTGG 1480
ACTTCCTTCAGGAGGTGAACATCTATGGAGTCACGGTGCC 1520
AGGGCACGAAGGCAGGGCAGGCATGGCGGCCTTGGCTCTG 1560
CGGCCCCCGCAGGCTCTGAACCTGGTGCAGCTCTACAGCC 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
ATGTTTCTGAGAACTTGCCACCGTATGCCCCACCTCGGTT 1640
TCTCAGGCTCCAGGAATCTTTGGCCACTACTGAGACCTTC 1680
AAACAGCAGAAGGTTAGGATGGCCAATGAGGGCTTTGACC 1720
CCAGTGTACTGTCTGACCCACTCTATGTTCTGGACCAAGA 1760
TATAGGGGCCTACCTGCCCCTCACACCTGCCCGGTACAGT 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
GCCCTCCTGTCTGGAGACCTTCGAATCTGAAACCTTCCAC 1840
TTGAGGGAGGGGCTCGGAGGGTACAGGCCACCATGGCTGC 1880
ACCAGGGAGGGTTTTCGGGTATCTTTTGTATATGGAGTCA 1920
TTATTTTGTATAAACAGCTGGAGCTTAAAAAAAAAAAAAA 1960
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 1998

```

Fig. 66B

65260"40550460

mmFATP3 partial.protein

...

10 20 30 40

ESSESGCSLAWRLAYLAREQPTHFLIHGAQRFSYAEAER 40
 ESNRIARAFLRARGWTGRRGSGRGSTEEGARVAPPAGDA 80
 AARGTTAPPLAPGATVALLLPAGPDFLWIWFGGLAKAGLRT 120
 AFVPTALRRGPLLHCLRSCGASALVLATEFLESLEPDLP 160
 LRAMGLHLWATGPETNVAGISNLLSEAADQVDEPVPGYLS 200

210 220 230 240

APQNIMDTCLYIFTSGTTGLPKAARISHLKVLQCQGFYHL 240
 CGVHQEDVIYLALPLYHMSGSLGIVGCLGIGATVVLKPK 280
 FSASQFWDDCQKHRVTVFQYIGELCRYLVNQPPSKAEFDH 320
 KVR LAVGSGLRPDTWERFLRRFGPLQILETYGMTEGNVAT 360
 FNYTGRQGAVGRASWLYKHIFPFSIRYDVMTEGPIRNAQ 400

410 420 430 440

GHCMTTSPGEPGLLVAPVSQQSPFLGYAGAPELAKDKLLK 440
 DVFWSGDVFFNTGDLLVCDEQGFLHFHRTGDTIRWKGEN 480
 VATTEVAEVLETDLFLQEVNIYGVTVPGHEGRAGMAALAL 520
 RPPQALNLVQLYSHVSENLPYARPRFLRLQESLATTETF 560
 KQKVRMANEGFDPVLSPLYVLDQDIGAYLPLTPARYS 600

610 620 630 640

ALLSGDLRI. 610

Fig. 67

mmFATP4 full length.DNA

10 20 30 40
 ATGCTGCTTGGAGCCTCTCTGGTGGGGGCGCTACTGTTCT 40
 CCAAGCTAGTGCTGAAGCTGCCCTGGACCCAGGTGGGATT 80
 CTCCTGTTGCTCCTGTACTTGGGGTCTGGTGGCTGGCGT 120
 TTCATCCGGGTCTTCATCAAGACGGTCAGGAGAGATATCT 160
 TTGGTGGCATGGTGCTCCTGAAGGTGAAGACCAAGGTGCG 200
 210 220 230 240
 ACGGTACCTTCAGGAGCGGAAGACGGTGCCCCTGCTGTTT 240
 GCTTCAATGGTACAGCGCCACCCGGACAAGACAGCCCTGA 280
 TTTTCGAGGGCACAGACACTCACTGGACCTTCCGCCAGCT 320
 GGATGAGTACTCCAGTAGTGTGGCCAACCTTCTGCAGGCC 360
 CGGGGCCTGGCCTCAGGCAATGTAGTTGCCCTCTTTATGG 400
 410 420 430 440
 AAAACCGCAATGAGTTTGTGGGTCTGTGGCTAGGCATGGC 440
 CAAGCTGGGCGTGGAGGGCGGCTCTCATCAACACCAACCTT 480
 AGGCGGGATGCCCTGCGCCACTGTCTTGACACCTCAAAGG 520
 CACGAGCTCTCATCTTTGGCAGTGAGATGGCCTCAGCTAT 560
 CTGTGAGATCCATGCTAGCCTGGAGCCCACTCAGCCTC 600
 610 620 630 640
 TTCTGCTCTGGATCCTGGGAGCCCAGCACAGTGCCCGTCA 640
 GCACAGAGCATCTGGACCCTCTTCTGGAAGATGCCCCGAA 680
 GCACCTGCCAGTCACCCAGACAAGGGTTTTACAGATAAG 720
 CTCTTCTACATCTACACATCGGGCACCACGGGGCTACCCA 760
 AAGCTGCCATTGTGGTGCACAGCAGGTATTATCGTATGGC 800
 810 820 830 840
 TTCCCTGGTGTACTATGGATTCCGCATGCGGCCTGATGAC 840
 ATTGTCTATGACTGCCTCCCCCTCTACCACTCAAGCAGGA 880
 AACATCGTGGGGATTGGCAGTGCTTACTCCACGGCATGAC 920
 TGTGGTGATCCGGAAGAAGTTCTCAGCCTCCCGGTTCTGG 960
 GATGATTGTATCAAGTACAACCTGCACAGTGGTACAGTACA 1000
 1010 1020 1030 1040
 TTGGCGAGCTCTGCCGCTACCTCCTGAACCAGCCACCCCG 1040
 TGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCACTGGGC 1080
 AACGGTCTCCGGCAGTCCATCTGGACCGACTTCTCCAGCC 1120
 GTTTCACATCCCCAGGTGGCTGAGTTCTATGGGGCCAC 1160
 TGAATGCAACTGTAGCCTGGGCAACTTTGACAGCCGGGTG 1200

Fig. 68A

66260-10550460

mmFATP4 full length.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
GGGGCCTGTGGCTTCAATAGCCGCATCCTGTCCTTTGTGT 1240
ACCCTATCCGTTTGGTACGTGTCAATGAGGATACCATGGA 1280
ACTGATCCGGGGACCCGATGGAGTCTGCATTCCCTGTCAA 1320
CCAGGTCAGCCAGGCCAGCTGGTGGGTCGCATCATCCAGC 1360
AGGACCCTCTGCGCCGTTTCGACGGGTACCTCAACCAGGG 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
TGCCAACAACAAGAAGATTGCTAATGATGTCTTCAAGAAG 1440
GGGGACCAAGCCTACCTCACTGGTGACGTCCTGGTGATGG 1480
ATGAGCTGGGTTACCTGTACTTCCGAGATCGCACTGGGGA 1520
CACGTTCCGCTGGAAAGGGGAGAATGTATCTACCACTGAG 1560
GTGGAGGGCACACTCAGCCGCCTGCTTCATATGGCAGATG 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
TGGCAGTTTATGGTGTGAGGTGCCAGGAAGTGAAGGCCG 1640
AGCAGGAATGGCTGCCGTTGCAAGTCCCATCAGCAACTGT 1680
GACCTGGAGAGCTTTGCACAGACCTTGAAAAAGGAGCTGC 1720
CTCTGTATGCCCGCCCCATCTTCTGCGCTTCTTGCTGA 1760
GCTGCACAAGACAGGGACCTTCAAGTTCCAGAAGACAGAG 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
TTGCGGAAGGAGGGCTTTGACCCATCTGTTGTGAAAGACC 1840
CGCTGTTCTATCTGGATGCTCGGAAGGGCTGCTACGTTGC 1880
ACTGGACCAGGAGGCCATACCCGCATCCAGGCAGGCGAG 1920
GAGAAGCTGTGATTTCCCCCTACATCCCTCTGAGGGCCAG 1960
AAGATGCTGGATTACAGAGCCCTAGCGTCCACCCCAGAGGG 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
TCCTGGGCAATGCCAGACCAAAGCTAGCAGGGCCCGCACC 2040
TCCGCCCCCTAGGTGCTGATCTCCCCTCTCCCAAAGTCCA 2080
AGTGACTCACTGCCGCTTCCCCGACCCCTCCAGAGGCTTTC 2120
TGTGAAAGTCTCATCAAAGCTGTGTCTTCTGGTCCAGGCG 2160
TGGCCCCCTGGCCCCAGGGTTTCTGATAGGCTCCTTTAGGA 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
TGGTATCTTGGGTCCAGCGGGCCAGGGTGTGGGAGAGGAG 2240
TCACTAAGATCCCTCCAATCAGAAGGGAGCTTACAAAGGA 2280
ACCAAGGCAAAGCCTGTAGACTCAGGAAGCTAAGTGGCCA 2320
GAGACTATAGTGGCCAGTCATCCCATGTCCACAGAGGATC 2360
TTGGTCCAGAGCTGCCAAAGTGTACCTCTCCCTGCCTGC 2400

      2410      2420      2430      2440
      | | | | | | | | | | | | | | | |
ACCTCTGGGGAAAAGAGGACAGCATGTGGCCACTGGGCAC 2440
CTGTCTCAAGAAGTCAGGATCACACACTCAGTCCTTGTTT 2480
CTCCAGGTTCCCTTGTTCTTGTCTCGGGGAGGGAGGGACG 2520
AGTGTCTGTCTGTCTTCTGCTGTGTGAGTCTGTG 2560
TTGCTTCTCCATCTGTCTAGCCTGAGTGTGGGTGGAACA 2600

```

Fig. 68B

66260"10550460

2610 2620 2630 2640
 GGCATGAGGAGAGTGTGGCTCAGGGGCCAATAAACTCTGC 2640
 CTTGACTCCTCTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2680
 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2710

Fig. 68C

[illegible]

mmFATP4 full length.protein

10 20 30 40
MLLGASLVGALLFSKLVKLKPWTQVGFSLLLLYLGSGGWR 40
FIRVFIKTVRRDIFGGMVLLKVTKVRRYLQERKTVPLLF 80
ASMVQRHPDKTALIFEGTDTHWTFRQLDEYSSSVANFLQA 120
RGLASGNVVALFMENRNEFVGLWLGMAKLGVEAALINTNL 160
RRDALRHCLDTSKARALIFGSEMASAICEIHASLEPTLSL 200
210 220 230 240
FCSGSWEPSTVPVSTEHLDPILLEDAPKHLPSHPDKGFTDK 240
LFYIYTS GTTGLPKAAIVVHSRYR MASLVYYGFRMRPDD 280
IVYDCLPLYHSSRKHRGDWQCL LHGMTVVIRKKFSASRFW 320
DDCIKYNCTVVQYIGELCRYLLNQPPREAESRHKVRMALG 360
NGLRQSIWTD FSSRFHIPQVAEFYGATECNC SLGNFDSRV 400
410 420 430 440
GACGFNSRILSFVYPIRLVRVNEDTMELIRGPDGVCIPCQ 440
PGQPGQLVGRIIQODPLRRFDGYLNQGANNKKIANDVFKK 480
GDQAYLTGDVLVMDDELGYLYFRDRTGDTFRWKGENVSTTE 520
VEGTLRLLHMADVAVYGVEVPGTEGRAGMAAVASPI SINC 560
DLESFAQTLKKELPLYARPIFLRFLPELHKTGTFKFQKTE 600
610 620 630 640
LRKEGFDPSVVKDPLFYLDARKGCYVALDQEAYTRIQAGE 640
EKL. 644

Fig. 69

mmFATP5 full length.DNA

1 10 20 30 40
 CACTCATCAGAGCTAAGAGAGACTACACGCTCTCATCTAC 40
 TTCAGAAAGAGCCAATGCCATGGGTATTTGGAAGAACTA 80
 ACCTTACTGCTGTTGCTGCTTCTGCTGGTTGGCCTGGGGC 120
 AGCCCCCATGGCCAGCAGCTATGGCTCTGGCCCTGCCTTG 160
 GTTCCTGGGAGACCCACATGCCTTGTGCTGCTTGGCTTG 200
 210 220 230 240
 GCATTGCTGGGCAGACCCTGGATCAGCTCCTGGATGCCCC 240
 ACTGGCTGAGCCTGGTAGGAGCAGCTCTTACCTTATTCCT 280
 ATTGCCTCTACAGCCACCCCCAGGGCTACGCTGGCTGCAT 320
 AAAGATGTGGCTTTTACCTTCAAGATGCTTTTCTATGGCC 360
 TAAAGTTCAGGCGACGCCTTAACAAACATCCTCCAGAGAC 400
 410 420 430 440
 CTTTGTGGATGCTTTAGAGCGGCAAGCACTGGCATGGCCT 440
 GACCGGGTGGCCTTGGTGTGTACTGGGTCTGAGGGCTCCT 480
 CAATCACAATAGCCAGCTGGATGCCAGGTCCTGTCAGGC 520
 AGCATGGGTCTGAAAGCAAAGCTGAAGGATGCCGTAATC 560
 CAGAACACAAGAGATGCTGCTGCTATCTTAGTTCTCCCGT 600
 610 620 630 640
 CCAAGACCATTCTGCTTTGAGTGTGTTTCTGGGGTTGGC 640
 CAAGTTGGGCTGCCCTGTGGCCTGGATCAATCCACACAGC 680
 CGAGGGATGCCCTTGCTACACTCTGTACGGAGCTCTGGGG 720
 CCAGTGTGCTGATTGTGGATCCAGACCTCCAGGAGAACCT 760
 GGAAGAAGTCCTTCCCAAGCTGCTAGCTGAGAACATTAC 800
 810 820 830 840
 TGCTTCTACCTTGGCCACAGCTCACCCACCCCGGGAGTAG 840
 AGGCTCTGGGAGCTTCCCTGGATGCTGCACCTTCTGACCC 880
 AGTACCTGCCAGCCTTCGAGCTACGATTAAGTGGAAATCT 920
 CCTGCCATATTCATCTTTACTTCAGGGACCACTGGACTCC 960
 CAAAGCCAGCCATCTTATCACATGAGCGGGTCATACAAGT 1000
 1010 1020 1030 1040
 GAGCAACGTGCTGTCCTTCTGTGGATGCAGAGCTGATGAT 1040
 GTGGTCTATGACGTCCTACCTCTGTACCATACGATAGGGC 1080
 TTGTCCTTGGATTCTTGGCTGCTTACAAGTTGGAGCCAC 1120
 CTGTGCTCTGGCCCCCAAGTTCTCTGCCTCCCGATTCTGG 1160
 GCTGAGTGCCGGCAGCATGGCGTAACAGTGATCTTGTATG 1200

Fig. 70A

mmFATP5 full length.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
TGGGTGAAATCCTGCGGTACTTGTGTAACGTCCCTGAGCA 1240
ACCAGAAGACAAGATACATACAGTGCGCTTGGCCATGGGA 1280
ACTGGACTTCGGGCAAATGTGTGGAAAACTTCCAGCAAC 1320
GCTTTGGTCCCATTCGGATCTGGGAATTCTACGGATCCAC 1360
AGAGGGCAATGTGGGCTTAATGAACTATGTGGGCCACTGC 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
GGGGCTGTGGGAAGGACCAGCTGCATCCTTCCAATGCTGA 1440
CTCCCTTTGAGCTTGTACAGTTCGACATAGAGACAGCAGA 1480
GCCTCTGAGGGACAAACAGGGTTTTTGCATTCTGTGGAG 1520
CCAGGAAAGCCAGGACTTCTTTTGACCAAGGTTCAAAGA 1560
ACCAACCTTCTCTGGGCTACCGTGGTTCACAGCCGAGTC 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
CAATCGGAACTTGTGCGAATGTACGACGCGTAGGAGAC 1640
CTGTACTTCAACACTGGGGACGTGCTGACCTTGGACCAGG 1680
AAGGCTTCTTCTACTTTCAAGACCGCCTTGGTGACACCTT 1720
CCGGTGGAAGGGCGAAAACGTATCTACTGGAGAGGTGGAG 1760
TGTGTTTTGTCTAGCCTAGACTTCCTAGAGGAAGTCAATG 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
TCTATGGTGTGCCTGTGCCAGGGTGTGAGGGTAAGGTTGG 1840
CATGGCTGCTGTGAAACTGGCTCCTGGGAAGACTTTTGAT 1880
GGGCAGAAGCTATACCAGCATGTCCGCTCCTGGCTCCCTG 1920
CCTATGCCACACCTCATTTTCATCCGTATCCAGGATTCCCT 1960
GGGATCACAAACACCTACAAGCTGGTAAAGTCACGGCTG 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
GTGCGTGAGGGTTTTGATGTGGGGATCATTGCTGACCCCC 2040
TCTACATACTGGACAACAAGGCCAGACCTTCCGGAGTCT 2080
GATGCCAGATGTGTACCAGGCTGTGTGTGAAGGAACCTGG 2120
AATCTCTGACCACCTAGCCAAGTGAAGGCAATCCAAAAG 2160
TGTAGAGATTGACACTAGTCAGCTTCACAAAGTTGTCCGG 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
GTTCCAGATGCCCATGGCCCAGTAGTACTTAGAGAAATAA 2240
CTTGAATGTGTATACAAAAA 2277

```

Fig. 70B

mmFATP5 full length.protein

10 20 30 40
 MGIWKKLTLLLLLLLLLVGLGQPPWPAAMALALRWFLGDPT 40
 CLVLLGLALLGRPWISSWMPHWLSLVGAALTFLPLQPP 80
 PGLRWLHKDVAFTFKMLFYGLKFRRRLNKHPPETFVDALE 120
 RQALAWPORVALVCTGSEGSSITNSQLDARSCQAAWVLKA 160
 KLKDAVIQNTRDAAAILVLPSKTISALSVFLGLAKLGCPV 200
 210 220 230 240
 AWINPHSRGMPLLHSVRSSGASVLIVDPDLQENLEEVLPK 240
 LLAENIHCFYLGHSSTPGVEALGASLDAAPSDVPASLR 280
 ATIKWKSPAIFIFTSGTTGLPKPAILSHERVIOVSNVLSF 320
 CGCRADDVVDVLPYHTIGLVLGFLGCLQVGATCVLAPK 360
 FSASRFWAECRQHGVTVILYVGEILRYLCNVPEQPEDKIH 400
 410 420 430 440
 TVRLAMGTGLRANVWKNFQQRFGPIRIWEFYGSTEGNVGL 440
 MNYVGHCGAVGRTSCILRMLTPFELVQFDIETAELRDKQ 480
 GFCIPVEPGKPGLLLTQVRKNQPFLLGYRGSQAESNRKLYA 520
 NVRRVGDLYFNTGDVLTLDQEGFFYFQDRLGDTFRWKGEN 560
 VSTGEVECVLSSLDLEEVDVYGVVPVPGCEGKVGMAAVKL 600
 610 620 630 640
 APGKTFDQKLYQHVRSWLPAYATPHFIRIQDSLEITNTY 640
 KLVKSRLVREGFDVGIADPLYILDNKAQTFRSLMPDVYQ 680
 AVCEGTWNL. 690

Fig. 71

005504-0239

10 20 30 40
GCTCTCTGGGCCTATATCAAGCTGCTGAGGTACACGAAGC 40
GCCATGAGCGGCTCAACTACACGGTGGCGGACGTCTTCGA 80
ACGAAATGTTTCAGGCCCATCCGGACAAGGTGGCTGTGGTC 120
AGTGAGACGCAACGCTGGACCTTCCGTCAGGTGAACGAGC 160
ATGCGAACAAGGTGGCCAATGTGCTGCAGGCTCAGGGCTA 200
210 220 230 240
CAAAAAGGGCGATGTGGTGGCCCTGTTGCTGGAGAACC GC 240
GCCGAGTACGTGGCCACCTGGCTGGGTCTCTCCAAGATCG 280
GTGTGATCACACCGCTGATCAACACGAATCTGCGCGGTCC 320
CTCCCTGCTGCACAGCATCACGGTGGCCCATTTGCTCGGCT 360
CTCATTTACGGCGAGGACTTCCTGGAAGCTGTCACCGACG 400
410 420 430 440
TGGCCAAGGATCTGCCAGCGAACCTCACACTCTTCCAGTT 440
CAACAACGAGAAACAACAACAGCGAGACGGAAGAACATA 480
CCGCAGGCCAAGAATCTGAACGCGCTGCTGACCACGGCCA 520
GCTATGAGAAGCCTAACAAGACGCAAGGTTAACCACCACGA 560
CAAGCTGGTCTACATCTACACCTCCGGCACCACAGGATTG 600
610 620 630 640
CCAAAGGCTGCGGTTATCTCTCACTCCCGTTATCTGTTTA 640
TCGCTGCTGGCATCCACTACACCATGGGTTTCCAGGAGGA 680
GGACATCTTCTACACGCCCTTGCCTTTGTACCACACCGCT 720
GGTGGCATTATGTGCATGGGTGAGTCGGTGCTCTTTGGCT 760
CCACGGTCTCCATTGCGAAGAAGTTCTCGGCATCCAATA 800
810 820 830 840
TTTCGCCGACTGCGCCAAGTATAATGCAACTATTGGTCAG 840
TATATCGGTGAGATGGCTCGCTACATTCTAGCTACGAAAC 880
CCTCGGAATACGACCAGAAACACCGAGTGGCTCTGGTCTT 920
TGGAAACGGACTGCGACCGCAGATTTGGCCACAGTTTGTG 960
CAGCGCTTCAACATTGCCAAGGTTGGCGAGTTCTACGGCG 1000
1010 1020 1030 1040
CCACCGAGGGTAATGCGAACATCATGAATCATGACAACAC 1040
GGTGGGCGCCATCGGCTTTGTGTGCGCGCATCCTGCCCAAG 1080
ATCTACCCAATCTCGATCATTCGCGCCGATCCGGACACCG 1120
GAGAGCCCATAGAGATAGGAATGGCCTATGCCAACTGTG 1160
CGCTCCCAACGAGCCAGGCGTATTTCATCGGCAAGATCGTC 1200

Fig. 72A

dmFATP partial.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
AAAGGAAATCCTTCTCGCGAATTCCTCGGATACGTCGATG 1240
AAAAGGCCTCCGCGAAGAAGATTGTTAAGGATGTGTTCAA 1280
GCATGGCGATATGGCTTTCATCTCCGGAGATCTGCTGGTT 1320
GCCGACGAGAAGGGTTATCTGTACTTCAAGGATCGCACCG 1360
GTGACACCTTCCGCTGGAAGGGCGAGAATGTTTCCACCAG 1400

      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
CGAGGTGGAGGCGCAAGTCAGCAATGTGGCCGGTTACAAG 1440
GATACCGTCGTTTACGGCGTAACCATTCGCACACCGAGG 1480
GAAGGGCCGGCATGGCCGCCATCTATGATCCGGAGCGAGA 1520
ATTGGACCTCGACGTCTTCGCCGCTAGCTTGGCCAAGGTG 1560
CTGCCCGCGTACGCTCGTCCCCAGATCATTGATTGCTCA 1600

      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
CCAAGGTGGACCTGACTGGAACCTTTAAGCTGCGCAAGGT 1640
AGACCTGCAGAAGGAGGGCTACGATCCGAACGCGATCAAG 1680
GACGCGCTGTACTACCAGACTTCCAAGGGTCGGTACGAGC 1720
TGCTCACGCCCCAGGTTTACGACCAGGTGCAGCGCAACGA 1760
AATCCGCTTCTAAGAGCTGCAATAGAGTTGTGTCTGAACC 1800

      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
TTGCCTTTTGCCCAATATGCTGTTAATTAGTTTGTAAGGC 1840
TAAGTGTAGTAGAGGAAAAATCGGGGGAAATCGGCAGCAAA 1880
GATCATTTCAGCCTAGGAGAGATGCATCCGAAGCACATTTC 1920
CATGTCAACAATGCACTTTTGTATATCGTAAGCATATATA 1960
TATCGTATATCGTAAACGTAGTTGTATCTGCATTTGTGTA 2000

      2010      2020      2030      2040
      | | | | | | | | | | | | | | | |
GATGATAGCCTCCTATACGCATTTCAATTGTTTTTAGCGT 2040
GCTAAAGAACCTTGTTAAATGCAATTTTCAGCTATTGTTTA 2080
GTCAGTTTTAGTGGCATTTCACATTCATTCTCGTTGCGT 2120
TTCGTTTTTGCCTGTACATATGAGAAGCTCTGATGTTTTT 2160
GTATCAAATAAAGTTTTTTTCTTCACCACGGACCACGTGA 2200

      2210      2220      2230      2240
      | | | | | | | | | | | | | | | |
AAAAAAAAAAAAAAAAAAAAA 2221

```

Fig. 72B

86260"4050460

dmFATP partial.protein

10 20 30 40
 ALWAYIKLLRYTKRHERLNYTVADVFERNVQAHPOKVAVV 40
 SETQRWTFRQVNEHANKVANVLQAQGYKKGDVVALLLENR 80
 AEYVATWLGLSKIGVITPLINTNLRGPSLLHSITVAHCSA 120
 LIYGEDFLEAVTDVAKDLPANLTLFQFNENNNSETEKNI 160
 PQAKNLNALLTTASYEKPNTQVNHHDKLVIYITSGTTGL 200
 210 220 230 240
 PKAAVISHSRYLFIAAGIHYTMGFQEEDIFYTPLPLYHTA 240
 GGIMCMGQSVLFGSTVSIRKKFSASNYFADCAKYNATIGQ 280
 YIGEMARYILATKPSEYDQKHRVRLVFGNGLRPQIWPQFV 320
 QRFNIAKVGEFYGATEGNANIMNHDNTVGAIGFVSRILPK 360
 IYPISIIRADPDTGEPIDRNLGLCOLCAPNEPGVFIGKIV 400
 410 420 430 440
 KGNPSREFLGYYDEKASAKKIVKDVFKHGDMAFISGDLLV 440
 ADEKGYLYFKDRTGDTFRWKGENVSTSEVEAQVSNVAGYK 480
 DTVVYGVITIPHTEGRAGMAAIYDPERELDLDFVFAASLAKV 520
 LPAYARPQIIIRLLTKVDLTGTFKLKRVLDLQKEGYDPNAIK 560
 DALYYQTSKGRYELLTPQVYDQVQRNEIRF 590

Fig. 73

66260"40550460

1 10 20 30 40
AGTGTAGATACCACAGGAACGTTTAAAATCCAGAAGACCA 40
GACTGCAAAGGGAAGGATACGATCCACGGCTCACAACCTGA 80
CCAGATCTACTTCCTAAACTCCAGAGCAGGGCGTTACGAG 120
CTTGTCAACGAGGAGCTGTACAATGCATTTGAACAAGGGC 160
AGGATTTCCCTTT 173

Fig. 74

drFATP partial.protein

10 20 30 40
 SVDTTGTGFKIQKTRLQREGYDPRLLTDDQIYFLNSRAGRYE 40
 LVNEELYNAFEQQGDFP 57

Fig. 75

[illegible]

10 20 30 40
 ATGAAGCTGGAGGAGCTTGTGACAGTTATGCTTCTCACAG 40
 TGGCTGTCATTGCTCAGAATCTCCGATTGGAGTAATATT 80
 GGCTGGAGTTCTTATTTTATACATCACAGTGGTTCATGGA 120
 GATTTCAATTTATAGAAGTTATCTTACGTTGAATAGGGATT 160
 TAACAGGATTGGCTCTAATTATTGAAGTCAAATCGACCT 200
 210 220 230 240
 ATGGTGGAGGTTGCATCAGAATAAAGGAATCCATGAACTG 240
 TTTTGGATATTGTGAAAAAGAATCCAAATAAGCCGGCGA 280
 TGATTGACATCGAGACGAATACAACAGAAACATACGCAGA 320
 GTTCAATGCACATTGTAATAGATATGCCAATTATTTCCAG 360
 GGTCTTGGCTATCGATCCGGAGACGTTGTCGCCTTGTACA 400
 410 420 430 440
 TGGAGAACTCGGTCGAGTTTGTGGCCGCGTGGATGGGACT 440
 CGCAAAAATCGGAGTTGTAACGGCTTGGATCAACTCGAAT 480
 TTGAAAAGAGAGCAACTTGTTTATTGTATCACTGCGAGCA 520
 AGACAAAGGCGATTATCACAAGTGTAACACTTCAGAATAT 560
 TATGCTTGATGCTATCGATCAGAAGCTGTTTGATGTTGAG 600
 610 620 630 640
 GGAATTGAGGTTTACTCTGTCTGGAGAGCCCAAGAAGAATT 640
 CTGGATTCAAGAATCTCAAGAAGAAGTTGGATGCTCAAAT 680
 TACTACGGAACCAAGACCCTTGACATAGTAGATTTTAAA 720
 AGTATTCTTTGCTTCATCTATACAAGTGGTACTACTGGAA 760
 TGCCAAAAGCCGCTGTCATGAAGCACTTCAGATATTACTC 800
 810 820 830 840
 GATTGCCGTTGGAGCCGCAAAATCATTCCGAATCCGCCCT 840
 TCTGATCGTATGTACGTCTCGATGCCAATTTATCACACTG 880
 CAGCTGGAATTCTTGGAGTTGGGCAAGCTCTGTTGGGTGG 920
 ATCATCGTGTGTCATTAGAAAAAATTCTCGGCTAGCAAC 960
 TTTTGGAGGGATTGTGTAAAGTATGATTGTACAGTTTCAC 1000
 1010 1020 1030 1040
 AATACATTGGAGAGATTTGTCTGGTACTTGTTGGCTCAGCC 1040
 AGTTGTGGAAGAGGAATCCAGGCATAGAATGAGATTGTTG 1080
 GTTGGAAACGGACTCCGTGCTGAAATCTGGCAACCATTTG 1120
 TAGATCGATTCCGTGTCAGAATTGGAGAACTTTATGGTTC 1160
 AACTGAAGGAACCTTCATCTCTCGTGAACATTGACGGACAT 1200

Fig. 76A

66260-10550460

[illegible]

Fig. 76B

ceFATPa coding only.protein

10 20 30 40
 MKLEELVTVMLLTVAVIAQNLPIGVILAGVLILYITVVHG 40
 DFIYRSYLTNRDLTGLALIEVKIDLWWRLHQNKGIEL 80
 FLDIVKKNPNKPAMIDIETNTTETAEFNAHCNRYANYFQ 120
 GLGYRSGDVVALYMENSVEFVAAWMGLAKIGVVTAWINSN 160
 LKREQLVHCITASKTKAIITSVTLQNIMLDAIDQKLFOVE 200
 210 220 230 240
 GIEVYSVGEPKKNSGFKNLKKKLDAGITTEPKTLDIVDFK 240
 SILCFIYTS GTTGMPKAAVMKHFRYYSIAVGAASFGIRP 280
 SDRMYVSMPIYHTAAGILGVGQALLGGSSCVIRKKFSASN 320
 FWRDCVKYDCTVSQYIGEICRYLLAQPVVEESRHRMRL 360
 VGNGLRAEIWQPFVDRFRVRIGELYGSTEGTSSLVNIDGH 400
 410 420 430 440
 VGACGFLPISPLTKKMHPVRLIKVDDVTGEAIRTSDGLCI 440
 ACNPGESGAMVSTIRKNNPLLOFEGYLNKKETNKKIIRDV 480
 FAKGDSCFLTGDLLHWORLGYVYFKDRTGDTFRWKGENVS 520
 TTEVEAILHPITGLSDATVYGVEVPQREGRVGMASVVRVV 560
 SHEEDETQFVHRVGARLASSLTSYAIPQFMRICQDVEKTG 600
 610 620 630 640
 TFKLVKTNLQRLGIMDAPSDSIYIYNSENRNFPFDNDLR 640
 CKVSLGSYPF. 651

Fig. 77

10 20 30 40
ATGAGGGAAATGCCGGACAGTCCCAAGTTTGC GTTAGTCA 40
CGTTTGTGTGTATGCAGTGGTTTTGTACAATGTCAACAG 80
CGTTTTCTGGAAATTTGTATTCATCGGATATGTTGTATTT 120
AGGCTGCTTCGCACTGATTTTGGAGAAGAGCACTTGCCA 160
CGTTACCTAGAGATTTTGC GGGACTGAAGCTCTTAATATC 200
210 220 230 240
GGTTAAGTCGACAATTCGTGGCTTGTTCAAGAAAGATCGC 240
CCAATTCATGAAATCTTTTGAATCAGGTGAAACAGCATC 280
CAAACAAAGTGGCGATTATTGAAATTGAAAGTGGTAGGCA 320
GTTGACGTATCAAGAATTGAATGCGTTAGCTAATCAGTAT 360
GCTAACCTTTACGTGAGTGAAGGTTACAAAATGGGCGACG 400
410 420 430 440
TTGTCGCTTTGTTTATGGAAAATAGCATCGACTTCTTTGC 440
AATTTGGCTGGGACTTTCCAAGATTGGAGTCGTGTCGGCG 480
TTCATCAACTCAAACCTGAAGTTGGAGCCATTGGCACATT 520
CGATTAATGTTTCGAAGTGCAAATCATGCATTACCAATAT 560
CAATCTGTTGCCGATGTTCAAAGCCGCTCGTGAAAAGAAT 600
610 620 630 640
CTGATCAGTGACGAGATCCACGTGTTTCTGGCTGGAAC TC 640
AGGTTGATGGACGTCATAGAAGTCTTCAGCAAGATCTCCA 680
TCTTTTCTCTGAGGATGAACCTCCAGTTATAGACGGACTC 720
AATTTTAGAAGCGTTCTGTGTTATATTTACACTTCCGGTA 760
CTACCGGAAATCCAAAGCCAGCCGTCATTAAACACTTCCG 800
810 820 830 840
TTACTTCTGGATTGCGATGGGAGCAGGAAAAGCATT TGGA 840
ATTAATAAGTCAGACGTTGTGTACATTACGATGCCAATGT 880
ATCACTCTGCCGCCGGTATCATGGGTATTGGATCATTAA T 920
TGCAATCGGGTCGACCGCTGTTATTAGGAAAAAGTTTTCG 960
GCAAGCAACTTCTGGAAAGATTGCGTCAAGTACAACGTCA 1000
1010 1020 1030 1040
CAGCGACACAGTACATTGGAGAAATCTGCAGGTATCTTCT 1040
GGCAGCGAATCCATGTCCTGAAGAGAAAACAACACAACGTG 1080
CGATTGATGTGGGGAAATGGTTTGAGAGGACAAATTTGGA 1120
AAGAGTTTGTAGGAAGA-TTTGGAATTAAGAAAATTGGAGA 1160
GTTGTACGGCTCAACAGAAGGAAACTCCAATATTGTTAAC 1200

Fig. 78A

Figure 6

Fig. 78B

ceFATPb coding only.protein _____

... 1

10 20 30 40
MREMPDSPKFALVTFVYAVVLYNVNSVFWKFVFIGYVVF 40
RLLRTDFGRRALATLPRDFAGLKLLISVKSTIRGLFKKOR 80
PIHEIFLNQVKQHPNKVAIIIEIESGRQLTYQELNALANQY 120
ANLYVSEGYKMGDVVALFMENSIDFFAIWLGLSKIGVSA 160
FINSNLKLEPLAHSINYSKCKSCITNINLLPMFKAAREKN 200
210 220 230 240
LISDEIHVFLAGTQVDGRHRSLOQDLHLFSEDEPPVIDGL 240
NFRSVLCYIYTS GTTGNPKPAVIKHFYFWIAMGAGKAFG 280
INKSDVVYITMPMYHSAAGIMGIGSLIAFGSTAVIRKKFS 320
ASNFWKDCVKYNVTATQYIGEICRYLLAANPCPEEKQHN 360
RLMWGNGLRGQIWKEFVGRFGIKKIGELYGSTEGNSNIVN 400
410 420 430 440
VDNHVGACGFMPPIYPHIGSLYPVRLIKVD RATGELERDKN 440
GLCVPCVPGETGEMVGVKEKDILLKFEGYVSEGDTAKKI 480
YRDVFKHGDVKVFASGDILHWDDLGYLYFVDRCGDTFRWKG 520
ENVSTTEVEGILQPVMDVEDATVYGVTVGKMEGRAGMAGI 560
VVKDGT DVEKFIADITSRLTENLASAIPVFIRLCKEVDR 600
610 620 630 640
TGTFKLKKTDLQKQGYDLVACKGDPIYYWSAAEKSYKPLT 640
DKMQQDIDTGVYDRI. 656

Fig. 79

040504-09260

10 20 30 40
 ATGGCGTGTATGCATCAGGCTCAGCTATACAATGATCTAG 40
 AGGAATTGCTAACTGGTCCATCAGTACCCATCGTTGCTGG 80
 AGCTGCTGGAGCTGCAGCTCTCACTGCCTACATTAACGCC 120
 AAATACCACATAGCCCATGATCTCAAGACCCTCGGTGGTG 160
 GATTGACACAATCGTCCGAAGCGATTGATTTCATAAACCG 200

210 220 230 240
 CCGCGTCGCACAAAAGCGCGTCTCAGCACCATCTTC 240
 CAGGAGCAGGTCCAAAAACAATCAAATCATCCCTTTCTTA 280
 TCTTTGAGGGCAAGACATGGTCTTACAAGGAGTTCTCTGA 320
 GGCATACACGAGGGTCGCGAACTGGCTGATTGATGAGCTG 360
 GACGTACAAGTAGGGGAGATGGTCGCAATTGATGGCGGAA 400

410 420 430 440
 ATAGTGCAGAGCACCTGATGCTTTGGCTTGCACTTGATGC 440
 AATCGGTGCGGCTACGAGTTTTTTGAACTGGAACCTGACA 480
 GGGGCAGGGTTAATTCATTGCATAAAGCTATGCGAATGTC 520
 GATTCGTTATCGCAGACATCGATATTAAAGCGAACATTGA 560
 ACCGTGCCGTGGCGAACTGGAGGAGACGGGCATCAACATT 600

610 620 630 640
 CACTACTATGACCCATCCTTCATCTCATCGCTACCGAATA 640
 ACACGCCAATTCCCGACAGCCGCACTGAGAACATTGAATT 680
 AGATTGAGTACGAGGACTGATATACACATCTGGAACCACT 720
 GGTCTACCTAAAGGCGTGTATATAAGCACTGGCCGCGAGC 760
 TTAGGACTGACTGGTCGATTTCAAAGTATCTAAATCTCAA 800

810 820 830 840
 GCCCACGGATCGAATGTATACATGTATGCCGCTCTACCAT 840
 GCCGCTGCACACAGCCTCTGTACAGCATCAGTTATTCATG 880
 GTGGAGGTACCGTGGTATTGAGCAGGAAATTCTCACACAA 920
 GAAGTTCTGGCCTGAAGTTGTGGCTTCGGAAGCAAATATC 960
 ATTCAGTACGTTGGTGAATTAGGTGATATCTCCTGAATG 1000

1010 1020 1030 1040
 GTCCAAAGAGTCCTTACGACAGGGCCCATAAAGTCCAGAT 1040
 GGCGTGGGGCAATGGCATGCGTCCAGACGTGTGGGAAGCG 1080
 TTTCTGTAACGCTTCAACATACCAATTATTCATGAGCTCT 1120
 ATGCCGCAACCGATGGGCTCGGGTCAATGACCAATCGTAA 1160
 CGCGGGCCCTTTTACAGCAAACGTATTGCGCTGCGAGGG 1200

Fig. 80A

THE UNIVERSITY OF CHICAGO

Fig. 80B

chFATP coding only.protein

10 20 30 40
MACMHQAQLYNDLEELLTGPSVPIVAGAAGAAALTAYINA 40
KYHIAHDLKTLGGGLTQSSEAIIDFINRRVAQKRVLTHHIF 80
QEQQVQKQSNHPFLIFEGKTWSYKEFSEAYTRVANWLIDEL 120
DVQVGEMVAIDGGNSAEHLMLWLALDAIGAATSFLNWNLT 160
GAGLIHCIKLCECRFVIADIDIKANIEPCRGELEETGINI 200
210 220 230 240
HYYDPSFISSLPNNTPIPDSTRTENIELDSVRGLIYTS GTT 240
GLPKGVIISTGRELRTDWSISKYLNKPTDRMYTCMP LYH 280
AAAHSLCTASVIHGGGTVVLSRKFSHKKFWPEVVASEANI 320
IQYVGELGRYLLNGPKSPYDRAHKVQMAWGNGMRPDVWEA 360
FRERFNIPIIHELYAATDGLGSMNTRNAGPFTANCIALRG 400
410 420 430 440
LIWHWKFRNQEVLVKMDLDTDEIMRDRNGFAIRCAVNEPG 440
QMLFRLTPETLAGAPSYNNETATQSRRITDVFQKGDLWF 480
KSGDMLRQDAEGRVYFVDRLGDTFRWKSENVSTNEVADV M 520
GTFPQIAETNVYGVLPVGNDRVRS LNCHGRRRDRVDIRF 560
AALAKHARDRLPGYAVPLFLRVTPALEYTGTLKIQKGRLK 600
610 620 630 640
QEGIDPDKISGEDKLYWLPPGSDIYLPFGKMEWQGIYDKR 640
IRL 643

Fig. 81

0040504-0050460

```

      10      20      30      40
      |      |      |      |
CTTTACCATTCATCAGCTTCATTCTGCATTTTATAGCTTGA 40
CGGCAGCCGGGTCTACGCTGATCATCGGCCGCAAGTTCTC 80
CGCGAGAACTTCATAAAGGAAGCGCGCGAGAACGACGCC 120
ACGGTCATCCAGTACGTGGGTGAGACCTTGCGATATCTGC 160
TCGCCACCCCCGGTGAAACCGATCCAGTTACTGGCGAAGA 200

      210      220      230      240
      |      |      |      |
CCTGGACAAAAAGCACAATATTCGAGCAGTATACGGCAAC 240
GGGCTACGGCCGGATATCTGGAACCGCTTCAAGGAGCGCT 280
TCAACGTGCCGACGGTTGCCGAATTTTATGCTGCAACCGA 320
GAGCCCAGGCGGAACATGGAACATTTCAACAAATGACTTC 360
ACTGCCGGAGCCATTGGGCACACTGGCGTGCTTAGTGGAT 400

      410      420      430      440
      |      |      |      |
GGCTTCTTGACGCGGCCTTACTATTGTGCGAGGTGGACCA 440
GGAATCACAGGAACCATGGCGCGATCCCCAAACCGGGTTC 480
TGCAAGCCGGTCCCGCGAGGCGAAGCAGGCGAGCTCCTGT 520
ATGCCATTGATCCGGCCGACCCGGGCGAGACCTTCCAGGG 560
CTACTACCGCAACTCCTTTAGAGCACACTGGCGGCCG 597

```

Fig. 82

aspergillus partial.protein

...
10 20 30 40
|-----|
LYHSSASFCIFSLTAAGSTLIIGRKFSARNFIKEAREND 40
TVIQYVGETLRYLLATPGETDPVTGEDLDKKHNIRAVYGN 80
GLRPDIWNRFKERFNVPTVAEFYAATESPGGTWNYSTNDF 120
TAGAIGHTGVLSGWLLGRGLTIVEVDQESQEPWRDPQTGF 160
CKPVPRGEAGELLYAIDPADPGETFQGYRNSFRAHWRP 199

Fig. 83

002260-10550460

```

      10      20      30      40
      |      |      |      |
GCAAAGGCCGACGCGTGGCTGCGGACGGGTAACGTGATCA 40
GGGCGGACAACGAAGGGCGACTCTTCTTCCACGACCGGAT 80
CGGAGACACGTTCCGATGGAAGGGAGAGACNGTCAGCACA 120
CAAGAGGTCAGTTTGGTGCTCGGACGACACGACTCAATCA 160
AGGAGGCCAACGTGTACGGCGTGACGGTGCCGAACCACGA 200

      210      220      230      240
      |      |      |      |
CGGGCGGGCCGGCTGCGCTGCGCTCACGCTATCAGACGCT 240
CTGGCGACTGAAAAGAAGCTGGGCGATGAGCTGCTAAAGG 280
GATTGGCTACTCACTCGTCGACTTCGCTTCCCAAGTTTGC 320
GGTGCCGCAGTTCCTACGGGTGGTGCGCGGCGAGATGCAG 360
TCAACGGGCACCAACAAGCAACAGAAGCACGACCTGAGGG 400

      410      420      430      440
      |      |      |      |
TGCAGGGTGTAGAGCCGGGCAAGGTGGGCGTAGACGAGGT 440
GTACTGGTTGCGGGGAGGGACATATGTACCATTCGGAACA 480
GAGGATTGGGATGGGTTGAAGAAGGGTCTGTGAAGTTGT 520
GA 522

```

Fig. 84

mgFATP partial.protein

10 20 30 40
AKADAWLRTGNVIRADNEGRLEFFHDIRIGDTFRWKGETVST 40
QEVSLVLGRHDSIKEANVYGVTVPNHDGRAGCAALTLSDA 80
LATEKKLGDELLKGLATHSSTSLPKFAVPOFLRVVRGEMQ 120
STGTNKQKKHDLRVQGVPEPGKVGVDVYWLRRGGTYVPFGT 160
EDWDGLKKGLVKL 173

Fig. 85

66E26D"70550460

10 20 30 40
ATGTCTCCCATACAGGTTGTTGTCTTTGCCTTGTCAAGGA 40
TTTTCTGTCTATTATTCAGACTTATCAAGCTAATTATAAC 80
CCCTATCCAGAAATCACTGGGTATCTATTTGGTAATTAT 120
TTTGATGAATTAGACCGTAAATATAGATACAAGGAGGATT 160
GGTATATTATTCCCTTACTTTTTGAAAAGCGTGTGTTTGTTA 200
210 220 230 240
TATCATTGATGTGAGAAGACATAGGTTTCAAACTGGTAC 240
TTATTTATTAAACAGGTCCAACAAAATGGTGACCATTTAG 280
CGATTAGTTACACCCGTCCCATGGCCGAAAAGGGAGAATT 320
TCAACTCGAAACCTTTACGTATATTGAACTTATAACATA 360
GTGTTGAGATTGTCTCATATTTTGCATTTTGATTATAACG 400
410 420 430 440
TTCAGGCCGGTGACTACGTGGCAATCGATTGTACTAATAA 440
ACCTCTTTTCGTATTTTTATGGCTTTCTTTGTGGAACATT 480
GGGGCTATTCCAGCTTTTTTAACTATAATACTAAAGGCA 520
CTCCGCTGGTTCACCTCCCTAAAGATTTCCAATATTACGCA 560
GGTATTTATTGACCCGTGATGCCAGTAATCCGATCAGAGAA 600
610 620 630 640
TCGGAAGAAGAAATCAAAAACGCACTTCTCTGATGTTAAAT 640
TAACTATCTTGAAGAACAAGACTTAATGCATGAACCTTTT 680
AAATTCGCAATCACCGGAATTCTTACAACAAGACAACGTT 720
AGGACACCATTAGGCTTGACCGATTTTAAACCTCTATGT 760
TAATTTATACATCTGGAACCACTGGTTTGCCTAAATCCGC 800
810 820 830 840
TATTATGTCTTGGAGAAAATCCTCCGTAGGTTGTCAAGTT 840
TTTGGTCATGTTTTACATATGACTAATGAAAGCACTGTGT 880
TCACAGCCATGCCATTGTTCCATTCAACTGCTGCCTTATT 920
AGGTGCGTGCGCCATTCTATCTCACGGTGTTGCCTTGCG 960
TTATCGCATAAATTTTCTGCCAGTACATTTTGGAAGCAAG 1000
1010 1020 1030 1040
TTTATTTAACAGGAGCCACGCACATCCAATATGTCGGAGA 1040
AGTCTGTAGATACCTGTTACATACGCCAATTTCTAAGTAT 1080
GAAAAGATGCATAAGGTGAAGGTTGCTTATGGTAACGGGC 1120
TGAGACCTGACATCTGGCAGGACTTCAGGAAGAGGTTCAA 1160
CATAGAAGTTATTGGTGAATTCTATGCCGCAACTGAAGCT 1200

Fig. 86A

scFATP coding only.DNA

```

      1210      1220      1230      1240
      | | | | | | | | | | | | | | | |
CCTTTTGCTACAACCTACCTTCCAGAAAGGTGACTTTGGAA 1240
TTGGCGCATGTAGGAACCTATGGTACTATAATTCAATGGTT 1280
TTTGTCAATCCAACAAACATTGGTAAGGATGGACCCAAAT 1320
GACGATTCCGTTATATATAGAAATTCCAAGGGTTTCTGCG 1360
AAGTGGCCCCCTGTTGGCGAACCAGGAGAAATGTTAATGAG 1400
      1410      1420      1430      1440
      | | | | | | | | | | | | | | | |
AATCTTTTTCCCTAAAAAACAGAAACATCTTTTCAAGGT 1440
TATCTTGGTAATGCCAAGGAAACAAAGTCCAAAGTTGTGA 1480
GGGATGTCTTCAGACGTGGCGATGCTTGGTATAGATGTGG 1520
AGATTTATTAAAGCGGACGAATATGGATTATGGTATTTT 1560
CTTGATAGAATGGGTGATACTTTCAGATGGAAATCTGAAA 1600
      1610      1620      1630      1640
      | | | | | | | | | | | | | | | |
ATGTTTCCACTACTGAAGTAGAAGATCAGTTGACGGCCAG 1640
TAACAAAGAACAATATGCACAAGTTCTAGTTGTTGGTATT 1680
AAAGTACCTAAATATGAAGGTAGAGCTGGTTTTGCAGTTA 1720
TTAAACTAACTGACAACTCTCTTGACATCACTGCAAAGAC 1760
CAAATTATTAAATGATTCCTTGAGCCGGTTAAATCTACCG 1800
      1810      1820      1830      1840
      | | | | | | | | | | | | | | | |
TCTTATGCTATGCCCCCTATTTGTTAAATTTGTTGATGAAA 1840
TTAAATGACAGATAACCTCATAAAATTTTGA 1872

```

Fig. 86B

scFATP coding only.protein

66260-10550460

10 20 30 40
MSPIQVVVFALSRIFLLLFRLIKLIITPIQKSLGYLFGNY 40
FDELDRKYRYKEDWYIIPYFLKSVFCYIIDVRRHRFQNWY 80
LFIKQVQONGDHLAISYTRPMAEKGEFQLETFTYIETYN 120
VLRLSHILHFDYNVQAGDYVAIDCTNKPLFVFLWLSLWNI 160
GAIPAFLNYNTKGTPLVHSLKISNITQVFIDPDASNPIRE 200
210 220 230 240
SEEEIKNALPDVKLNYLEEQDLMHELLNSQSPEFLQQDNV 240
RTPLGLTDFKPSMLIYTSGTTGLPKSAIMSWRKSSVGCQV 280
FGHVLHMTNESTVFTAMPLFHSTAALLGACAILSHGGCLA 320
LSHKFSASTFWKQVYLTGATHIQYVGEVCRYLLHTPIISKY 360
EKMHKVKVAYGNGLRPDIWQDFRKRFNIEVIGEFYAATEA 400
410 420 430 440
PFATTTFQKGDFGIGACRNYGTIIQWFLSFQQTIVRMDPN 440
DDSVIYRNSKGFCEVAPVGEPGEMLMRIFFPKKPETSFGQ 480
YLGNAKETKSKVVRDVFRRGDAWYRCGDLKADEYGLWYF 520
LDRMGDTFRWKSENVSTTEVEDQLTASNKEQYAQVLVVG 560
KVPKYEGRAGFAVIKLTDNSLDITAKTKLLNDSLSRLNLP 600
610 620 630 640
SYAMPLFVKFVDEIKMTDNLIK. 624

Fig. 87

10 20 30 40
 GTGTCCGATTACTACGGCGGCGCACACACAACGGTCAGGC 40
 TGATCGACCTGGCAACTCGGATGCCGCGAGTGTTGGCGGA 80
 CACGCCGGTGATTGTGCGTGGGGCAATGACCGGGCTGCTG 120
 GCGCGCCGAATTCCAAGGCGTCGATCGGCACGGTGTTCC 160
 AGGACCGGGCCGCTCGCTACGGTGACCGAGTCTTCCTGAA 200
 210 220 230 240
 ATTCGGCGATCAGCAGCTGACCTACCGCGACGCTAACGCC 240
 ACCGCCAACCGGTACGCCGCGGTGTTGGCCGCCGCGGCG 280
 TCGGCCCCGGCGACGTGCTTGGCATCATGTTGCGTAACTC 320
 ACCCAGCACAGTCTTGGCGATGCTGGCCACGGTCAAGTGC 360
 GCGGCTATCGCCGGCATGCTCAACTACCACCAGCGCGGCG 400
 410 420 430 440
 AGGTGTTGGCGCACAGCCTGGGTCTGCTGGACGCGAAGGT 440
 ACTGATCGCAGAGTCCGACTTGGTCAGCGCCGTCGCCGAA 480
 TGCGGCGCCTCGCGCGGCCGGGTAGCGGGCGACGTGCTGA 520
 CCGTCGAGGACGTGGAGCGATTGCCACAACGGCGCCCGC 560
 CACCAACCGGCGTCCGCGTCCGCGGTGCAAGCCAAAGAC 600
 610 620 630 640
 ACCGCGTTCTACATCTTCACCTCGGGCACCACCGGATTTT 640
 CCAAGGCCAGTGTCATGACGCATCATCGGTGGCTGCGGGC 680
 GCTGGCCGTCTTCGGAGGGATGGGGCTGCGGCTGAAGGGT 720
 TCCGACACGCTCTACAGCTGCCTGCCGCTGTACCACAACA 760
 ACGCGTTAACGGTCGCGGTGTCGTGCGGTGATCAATTCTGG 800
 810 820 830 840
 GGCGACCCTGGCGCTGGGTAAGTCGTTTTCGGCGTCGCGG 840
 TTCTGGGATGAGGTGATTGCCAACCAGGCGACGGCGTTTC 880
 TCTACATCGGCGAAATCTGCCGTTATCTGCTCAACCAGCC 920
 GGCCAAGCCGACCGACCGTGCCACCAGGTGCGGGTGATC 960
 TGCGGTAACGGGCTGCGGCCGGAGATCTGGGATGAGTTCA 1000
 1010 1020 1030 1040
 CCACCCGCTTCGGGGTCGCGCGGGTGTGCGAGTTCTACGC 1040
 CGCCAGCGAAGGCAACTCGGCCTTTATCAACATCTTCAAC 1080
 GTGCCCAGGACCGCCGGGGTATCGCCGATGCCGCTTGCCT 1120
 TTGTGGAATACGACCTGGACACCGGCGATCCGCTGCGGGA 1160
 TGCGAGCGGGCGAGTGCGTCGGGTACCCGACGGTGAACCC 1200

Fig. 88A

09405504.09239

SECRET

Fig. 88B

mtFATP coding only.protein

10 20 30 40
MSDYYGGAHTTVRLIDLATRMPRVLADTPVIVRGAMTGLL 40
ARPNKASIGTVFQDRAARYGDRVFLKFGDQQLTYRDANA 80
TANRYAAVLAARGVGPGDVVGIMLRNSPSTVLAMLATVKC 120
GAIAGMLNYHQGEVLAHSLGLLDAKVLIAESDLVSAVAE 160
CGASRGRVAGDVLTVEDVERFATTAPATNPASASAVQAKD 200
210 220 230 240
TAFYIFTSGTTGFPKASVMTHHRWLRALAVFGGMGLRLKG 240
SDTLYSCLPLYHNNALTAVVSSVINSGLATLALGKSFSASR 280
FWDEVIANRATAFVYIGEICRYLLNQPAKPTDRAHQVRVI 320
CGNGLRPEIWDEFTTRFGVARVCEFYAASEGNSAFINIFN 360
VPRTAGVSPMPLAFVEYDLDTGDPLRDASGRVRRVDPGEP 400
410 420 430 440
GLLLSRVNRLQPFQGYTDPVASEKKLVRNAFRDGDWCFNT 440
GDVMSPOGMGHAAFVDRLGDTFRWKGENVATTQVEAALAS 480
DQTVEECTVYGVQIPRTGGRAGMAAITLRAGAEFDGQALA 520
RTVYGHLPGYALPLFVRVVGSLAHTTTFKSRKVELRNQAY 560
GADIEDPLYVLGPDEGYVPYYAEYPEEVSLGRRPQG. 598

Fig. 89

66260-4050460

Gene "H050450"

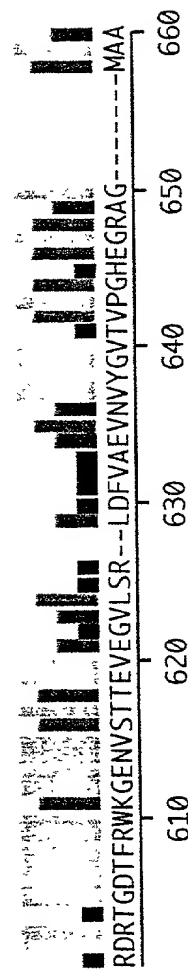
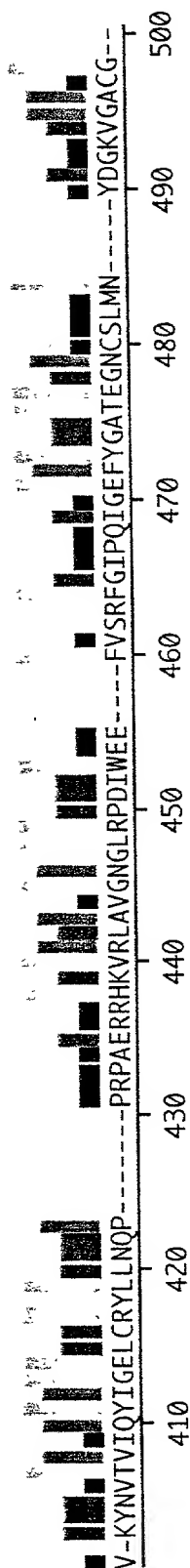
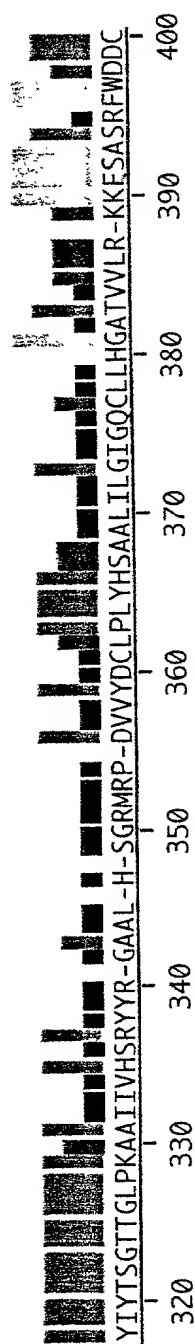


Figure 90

hsVLACS full length protein

hsVLACS full length protein

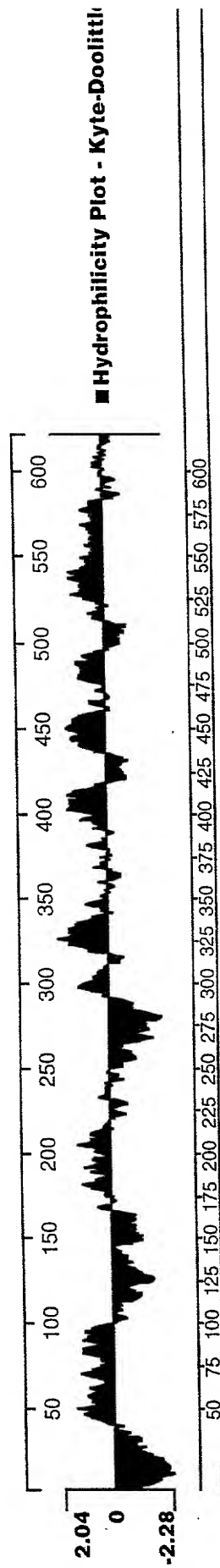


Figure 91

62260"40550450

hsFATP3partial.protein

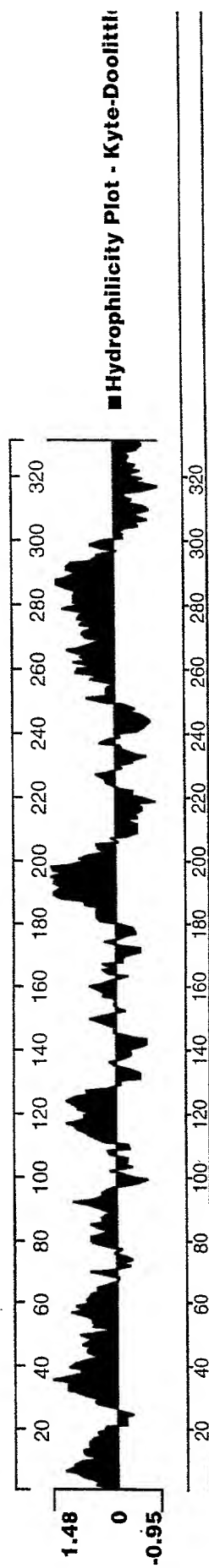


Figure 92

66260"10530450

hsFATP5partial.protein

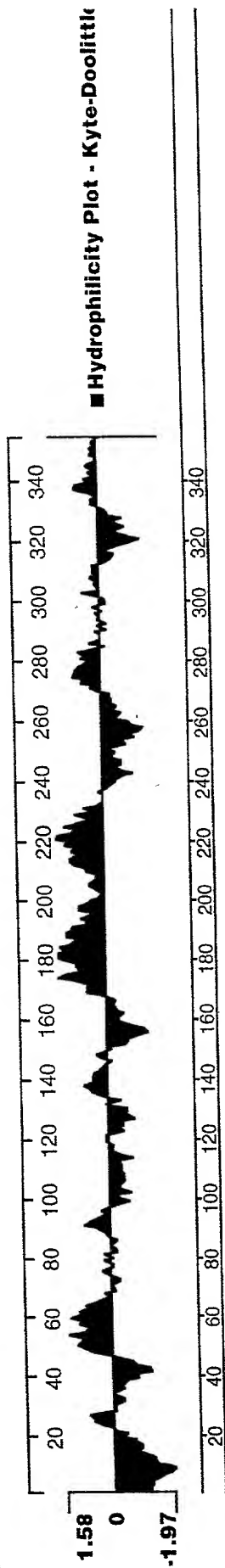


Figure 93

hsFATP3

```

1      oga ccc acg cgt ccg ggg atg ttt gcg agc ggc tgg aac cag acg gtg ccg ata gag gaa
1      M F A S G W N Q T V P I E E

61     gcg ggc tcc atg gct gcc ctc ctg ctg ctg ccc ctg ctg ctg ttg cta ccg ctg ctg ctg
15     A G S M A A L L L L P L L L L L P L L L

121    ctg ctg aag cta cac ctc tgg ccg cag ttg cgc tgg ctt ccg gcg gac ttg gcc ttt gcg
35     L L K L H L W P Q L R W L P A D L A F A

181    gtg cga gct ctg tgc tgc aaa agg gct ctt cga gct cgc gcc ctg gcc gcg gct gcc gcc
55     V R A L C C K R A L R A R A L A A A A A

241    gac ccg gaa ggt ccc gag ggg ggc tgc agc ctg gcc tgg cgc ctc gcg gaa ctg gcc cag
75     D P E G P E G G C S L A W R L A E L A Q

301    cag cgc gcc gcg cac acc ttt ctc att cac ggc tcg cgg cgc ttt agc tac tca gag gcg
95     Q R A A H T F L I H G S R R F S Y S E A

361    gag cgc gag agt aac agg gct gca cgc gcc ttc cta cgt gcg cta gcc tgg gac tgg gga
115    E R E S N R A A R A F L R A L G W D W G

421    ccc gac ggc ggc gac agc ggc gag ggg agc gct gga gaa ggc gag ccg gca gcg ccg gga
135    P D G G D S G E G S A G E G E R A A P G

481    gcc gga gat gca gcg gcc gga agc ggc gcg gag ttt gcc gga ggg gac ggt gcc gcc aga
155    A G D A A A G S G A E F A G G D G A A R

541    ggt gga gga gag ccc gcc gcc cct ctg tca cct gga gca act gtg gcg ctg ctc ctc ccc
175    G G G E P A A P L S P G A T V A L L L P

601    gct gcc cca gag ttt ctg tgg ctc tgg ttc ggg ctg gcc aag gcc gcc ctg cgc act gcc
195    A G P E F L W L W F G L A K A G L R T A

661    ttt gtg ccc acc gcc ctg cgc cgg ggc ccc ctg ctg cac tgc ctc cgc agc tgc ggc gcg
215    F V P T A L R R G P L L H C L R S C G A

721    cgc gcg ctg gtg ctg gcg cca gag ttt ctg gag tcc ctg gag ccg gac ctg ccc gcc ctg
235    R A L V L A P E F L E S L E P D L P A L

781    aga gcc atg ggg ctc cac ctg tgg gct gca ggc cca gga acc cac cct gct gga att agc
255    R A M G L H L W A A G P G T H P A G I S

841    gat ttg ctg gct gaa gtg tcc gct gaa gtg gat ggg cca gtg cca gga tac ctc tct tcc
275    D L L A E V S A E V D G P V P G Y L S S

901    ccc cag agc ata aca gac acg tgc ctg tac atc ttc acc tct ggc acc acg ggc ctc ccc
295    P Q S I T D T C L Y I F T S G T T G L P

961    aag gct gct ccg atc agt cat ctg aag atc ctg caa tgc cag ggc ttc tat cag ctg tgt
315    K A A R I S H L K I L Q C Q G F Y Q L C

1021   ggt gtc cac cag gaa gat gtg atc tac ctc gcc ctc cca ctc tac cac atg tcc ggt tcc
335    G V H Q E D V I Y L A L P L Y H M S G S

1081   ctg ctg ggc atc gtg ggc tgc atg ggc att ggg gcc aca gtg gtg ctg aaa tcc aag ttc
355    L L G I V G C M G I G A T V V L K S K F

1141   tcg gct ggt cag ttc tgg gaa gat tgc cag cag cac agg gtg acg gtg ttc cag tac att
375    S A G Q F W E D C Q Q H R V T V F Q Y I

1201   ggg gag ctg tgc cga tac ctt gtc aac cag ccc ccg agc aag gca gaa cgt ggc cat aag
395    G E L C R Y L V N Q P P S K A E R G H K

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Figure 94A

1261 gtc cgg ctg gca gtg ggc agc ggg ctg cgc cca gat acc tgg gag cgt ttt gtg cgg cgc
415 V R L A V G S G L R P D T W E R F V R R

1321 ttc ggg ccc ctg cag gtg ctg gag aca tat gga ctg aca gag ggc aac gtg gcc acc atc
435 F G P L Q V L E T Y G L T E G N V A T I

1381 aac tac aca gga cag cgg ggc gct gtg ggg cgt gct tcc tgg ctt tac aag cat atc ttc
455 N Y T G Q R G A V G R A S W L Y K H I F

1441 ccc ttc tcc ttg att cgc tat gat gtc acc aca gga gag cca att cgg gac ccc cag ggg
475 P F S L I R Y D V T T G E P I R D P Q G

1501 cac tgt atg gcc aca tct cca ggt gag cca ggg ctg ctg gtg gcc ccg gta agc cag cag
495 H C M A T S P G E P G L L V A P V S Q Q

1561 tcc cca ttc ctg ggc tat gct ggc ggg cca gag ctg gcc cag ggg aag ttg cta aag gat
515 S P F L G Y A G G P E L A Q G K L L K D

1621 gtc ttc cgg cct ggg gat gtt ttc ttc aac act ggg gac ctg ctg gtc tgc gat gac caa
535 V F R P G D V F F N T G D L L V C D D Q

1681 ggt ttt ctc cgc ttc cat gat cgt act gga gac acc ttc agg tgg aag ggg gag aat gtg
555 G F L R F H D R T G D T F R W K G E N V

1741 gcc aca acc gag gtg gca gag gtc ttc gag gcc cta gat ttt ctt cag gag gtg aac gtc
575 A T T E V A E V F E A L D F L Q E V N V

1801 tat gga gtc act gtg cca ggg cat gaa ggc agg gct gga atg gca gcc cta gtt ctg cgt
595 Y G V T V P G H E G R A G M A A L V L R

1861 ccc ccc cac gct ttg gac ctt atg cag ctc tac acc cac gtg tct gag aac ttg cca cct
615 P P H A L D L M Q L Y T H V S E N L P P

1921 tat gcc cgg ccc cga ttc ctc agg ctc cag gag tct ttg gcc acc aca gag acc ttc aaa
635 Y A R P R F L R L Q E S L A T T E T F K

1981 cag cag aaa gtt cgg atg gca aat gag ggc ttc gac ccc agc acc ctg tct gac cca ctg
655 Q Q K V R M A N E G F D P S T L S D P L

2041 tac gtt ctg gac cag gct gta ggt gcc tac ctg ccc ctc aca act gcc cgg tac agc gcc
675 Y V L D Q A V G A Y L P L T T A R Y S A

2101 ctc ctg gca gga aac ctt cga atc tga gaa ctt cca cac ctg agg cac ctg aga gag gaa
695 L L A G N L R I *

2161 ctc tgt

Figure 94B

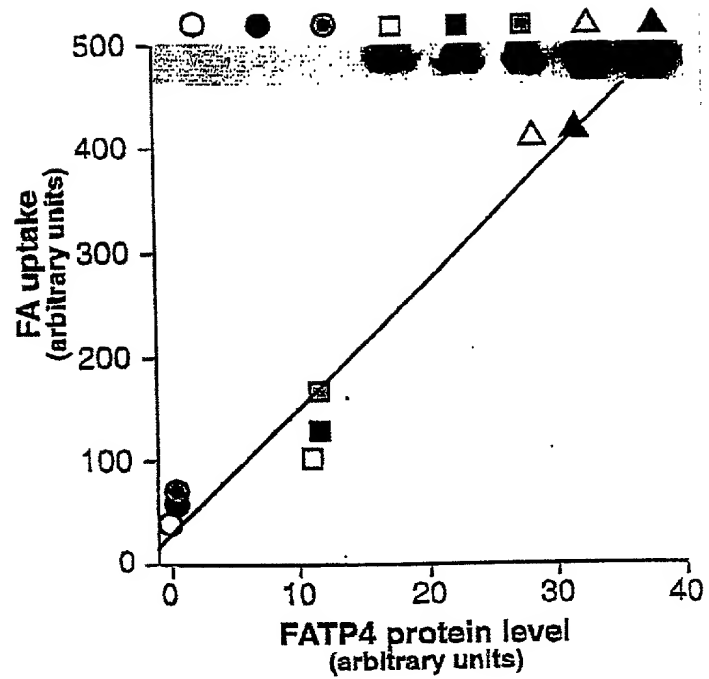


Figure 95

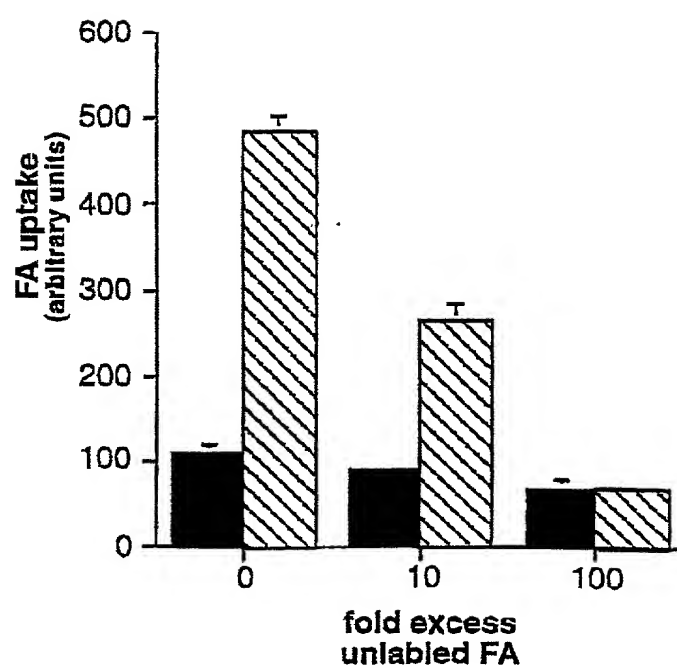


Figure 96

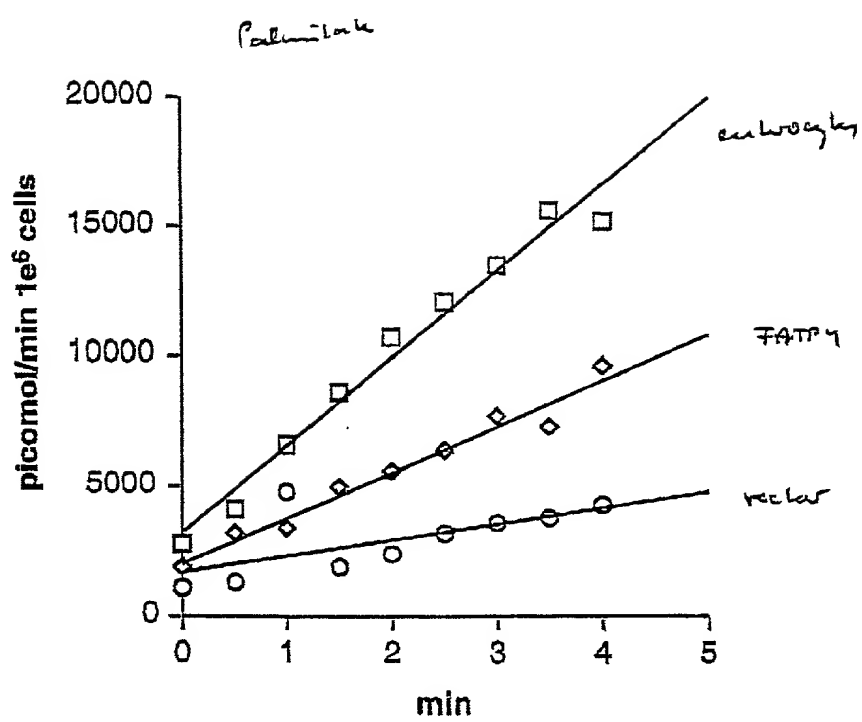


Figure 97

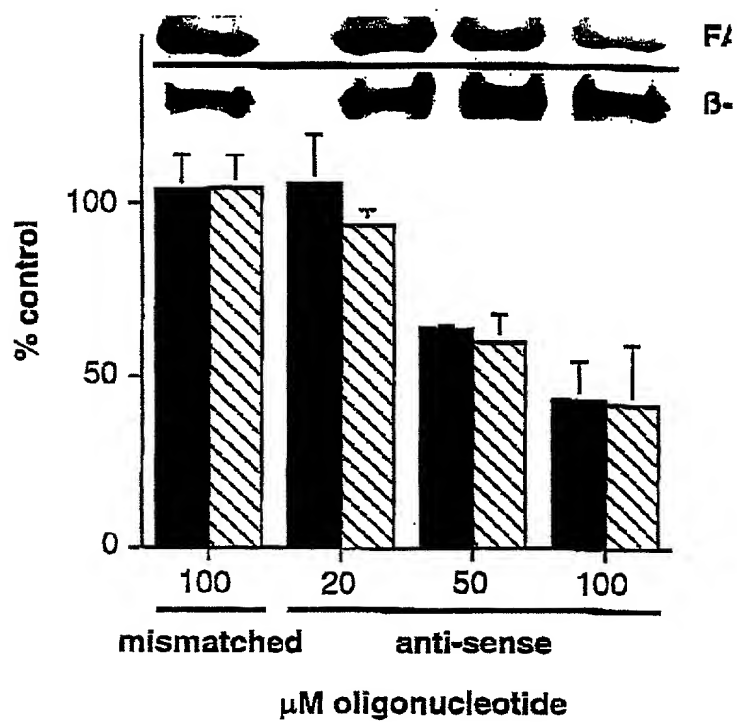


Figure 98

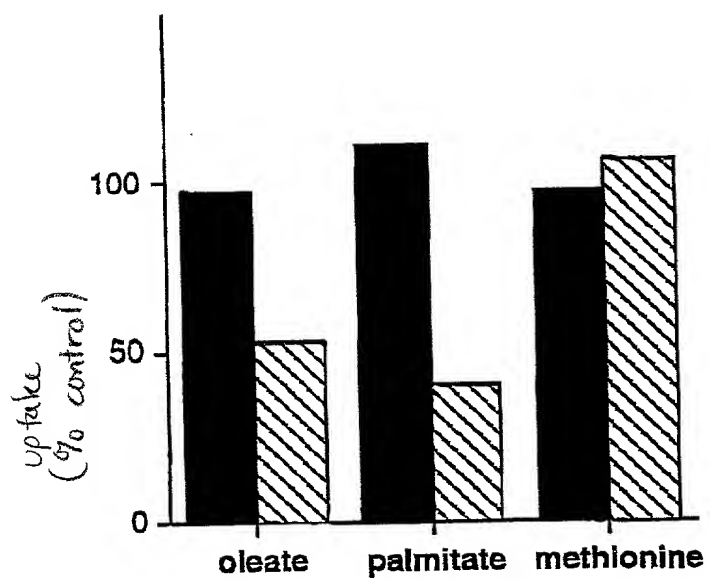


Figure 99